Cumulative Dissertation

Indicators of Medical Outcome in Inpatient Rehabilitation, Considering Routine Outcome Measures, Cardiac Autonomic Control and Dynamic Temporal Changes

submitted by

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Declaration

I hereby declare that this thesis is my own original work and that I have fully acknowledged by name all of those individuals and organizations that have contributed to the research for this thesis. Due acknowledgement has been made in the text to all other material used. Throughout this thesis and in all related publications, I followed the "Standards of Good Scientific Practice and Ombuds Committee at the Medical University of Graz".

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I. Disclosures

Parts of this thesis have been published (1-5) or have been submitted for publication (a, b).

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2. Grote, V., Böttcher, E., Mur, E., Kullich, W., Puff, H. (2019). Medizinische Ergebnisqualität: Unspezifische Outcome-Parameter einer stationären Rehabilitation des Stütz- und Bewegungsapparates in Österreich. [Medical Quality Outcomes: Unspecific Outcome Parameters of an Inpatient Musculoskeletal System Rehabilitation in Austria]. Phys Med Rehab Kuror, 29(02), 104-117. doi:10.1055/a-0835-6481
3. Grote, V., Unger, A., Puff, H., Böttcher, E. What to Expect: Medical Quality Outcomes and Achievements of a Multidisciplinary Inpatient Musculoskeletal System Rehabilitation. In: Bernardo-Filho M, Sá-Caputo D, Taiar R, editors. Physical Therapy Effectiveness [Working Title]: IntechOpen; 2019, online first. p. 27. doi:10.5772/intechopen.89596
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Submitted Manuscripts

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I confirm that all co-authors have explicitly agreed to the use of their data in this thesis, and I confirm that I have obtained permission to reproduce figures and tables[1,2].

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III. Abbreviations

ADL	Activities of daily living
ANS	Autonomic nervous system
BMI	Body Mass Index
CI	Confidence interval
d	Cohen's *d*
EQ-VAS	Subjective health status (0–100%)
GQG	*Gesundheitsqualitätsgesetz* [‘Austrian Federal Quality of Healthcare Act’]
GVA	*Gesundheitsvorsorge Aktiv* [‘Health Care Active’]
HRV	Heart rate variability
ICD	International Statistical Classification of Diseases
IND	Indication (orthopedic, cardiovascular, metabolic, oncology, pulmonary)
ISI	Indication specific index (*z*-means of homogeneous med. fields)
IV	Initial value/s (baseline, pre)
MED	Medical
MQO	Medical quality outcome (MQO_{idx}, average UHI and ISI)
PA	Physical activity
SMD	Standardized mean difference (d)
UHI	Unspecific Health Index (average of MED1-3)
VAS	Visual Analogue Scale

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Zusammenfassung

Einleitung: Die Häufigkeit chronischer Krankheiten nimmt in der modernen Gesellschaft und mit zunehmendem Alter zu. Die Rehabilitation spielt eine entscheidende Rolle bei der Verhinderung und Minimierung der mit dem Altern und chronischen Erkrankungen verbundenen funktionellen Einschränkungen. Medizinische Referenzdaten von unspezifischen und krankheitsspezifischen Gesundheitsindikatoren einer Rehabilitation sind nicht verfügbar.

Methoden: In Österreich wird eine Rehabilitation der Phase II (WHO) in der Regel stationär durchgeführt. Im Rahmen der Dokumentation von Patienten ist eine standardisierte Erhebung von Leistungsindikatoren zu individuellen Rehabilitationsergebnissen obligatorisch. Aus der Routinedokumentation werden zwei allgemeine medizinische Erfolgsindikatoren für die multidisziplinäre Rehabilitation definiert, ein unspezifischer und ein krankheitsspezifischer Gesundheitsindikator. Routinedaten von 24.414 Patienten mit unterschiedlichen medizinischen Diagnosen (57,9 ± 12,4 Jahre, 48,5% Frauen) werden statistisch aufbereitet. 37% dieser Patienten waren älter als 61+ Jahre. Weitere Ergebnisse spezifischer klinischer Substichproben werden vorgestellt.

Ergebnisse: Die stationäre Rehabilitation reduziert die mit dem Lebensstil verbundenen Risikofaktoren, optimiert die Organfunktion und verbessert das Wohlbefinden bei der Mehrheit der Patienten (78,8%). Medizinische Ausgangswerte zu Beginn der Rehabilitation sind alters- und geschlechtsabhängig. Rehabilitation führt zu den größten positiven Veränderungen in einer frühen Rehabilitationsphase und bei älteren Patienten (61+ Jahre). Verbesserungen treten dabei in zwei unabhängigen Bereichen auf, allgemeinen Gesundheitsparametern (Risikofaktoren) sowie krankheitsspezifischen Indikatoren. Diese Hauptkomponenten verhalten sich unterschiedlich, zeigen jedoch Verbesserungen in ähnlicher Größenordnung über verschiedene medizinische Indikationen hinweg.

Schlussfolgerungen: In dieser Arbeit werden klinische Referenzdaten bereitgestellt und deren dynamische zeitliche Veränderungen bei einer stationären Rehabilitation veranschaulicht. Das kann dazu genützt werden, Erfolgsraten und Nachhaltigkeit von Rehabilitationsbehandlungen zu verbessern, neue Behandlungsalternativen oder Umfeldbedingungen zu prüfen oder eine empirisch fundierte Bewertung der Ergebnisqualität von unterschiedlichen Behandlungspfaden vorzunehmen. Auf diese Weise kann ein standardisierter Einsatz routinemäßiger Ergebniskennwerte einen wertvollen Beitrag zum Qualitätsmanagement leisten.

Schlüsselwörter: *Stationäre Rehabilitation, Medizinische Ergebnisqualität, Routinedaten, Chronische Erkrankungen, Einflussfaktoren, Lebensalter, unspezifische und krankheits-spezifische Gesundheitsindikatoren, Referenzwerte;*

Abstract

Introduction: The incidence of chronic diseases is increasing in modern society and with age. Rehabilitation plays a critical role in preventing and minimizing the functional limitations associated with ageing and chronic conditions. Results of medical routine outcomes from rehabilitation are unavailable.

Methods: In Austria, phase II (WHO) rehabilitation is generally carried out as an inpatient. As part of the documentation for all patients who benefit from rehabilitation, the standardized collection of data relating to performance indicators for medical quality outcomes is obligatory. We define two general medical success indicators for multidisciplinary rehabilitation that can be obtained from routine documentation: an unspecific general health and a disease-specific indicator. Routine data from 24,414 patients with different medical diagnoses (57.9 ± 12.4 years, 48.5% women) were statistically analyzed. Thirty-seven percent of these patients were older than 61+ years. Further results of individual specific clinical samples are presented.

Results: The findings show that inpatient rehabilitation setting reduced lifestyle-related risk factors, optimized organ functioning and improved well-being in the majority of patients (78.8%). Medical initial values at the beginning of rehabilitation were age- and sex-related. Rehabilitation contributed to the greatest number of observed positive changes during the early rehabilitation stage and in older patients (61+ years). Improvements were observed in two independent areas: general health determinants (risk factors) and disease-specific indicators. These main components developed differently after the primary medical intervention, but showed similar improvements due to rehabilitation for various indications.

Conclusions: In this work, we provide clinical reference data and illustrate dynamic temporal trends in data related to inpatient rehabilitation. These results can be used to improve the success rates and sustainability of rehabilitation treatments, to examine new treatment alternatives or environmental conditions, or to make an evidence-based assessment of medical quality outcomes for different treatment pathways. In this way, a standardized use of routine outcome measures can provide a valuable contribution to quality assurance and evaluation.

Keywords: *Inpatient rehabilitation, medical quality outcome, routine outcome measurement, chronic diseases, influencing factors, age, unspecific and disease-specific health indicators, reference data*

1. Introduction

The World Health Organization (WHO) published five health strategies (promotion, prevention, cure, rehabilitation and palliative care) to achieve and maintain population health. In this publication, rehabilitation is described as an attempt to restore functioning that is affected by diseases, injuries, or other health conditions, ameliorate the impact of the reduction in capacity and minimize further initial health problems that arise as a result of environmental interactions (6). Special care in rehabilitation is given to typical ailments encountered in modern society, such as physical inactivity, obesity, alcohol abuse, smoking and inadequate nutrition (7-16).

The prevalence of severely disabling conditions and the absolute number of associated years lived with disability (YLDs) have increased dramatically over the last decade (17-19). According to the Global Burden of Diseases report (20-22), 39.8–40.5 million deaths occur each year due to non-communicable diseases in four main categories. These include cardiovascular, metabolic, oncology and pulmonary diseases, which are responsible for 63% of all global death. The prevalence of the leading cause of death, cardiovascular disease, increases with age: Forty percent of people over the age of 80 years suffer from cardiovascular diseases (23). Metabolic diseases are present, varying from insulin resistance, abdominal obesity and hypertensions to hyperlipidemia. In the US, one-third of the population suffers from a metabolic syndrome (24). There is also a high prevalence of degenerative diseases of the musculoskeletal system (25-28). The most common symptom is back pain [60-80% long-term prevalence (29, 30)], with a rise in prevalence with age. The highest prevalence for back pain occurs in individuals between 40-69 years; women are more frequently affected than men (31, 32). Cancer cases are also still increasing, with about 28% population affected in the last ten years. Respiratory diseases account for more than 10% of all disability-adjusted life years and rank second in terms of mortality after cardiovascular diseases (33).

The current results for Austria (34) agree with the results of international studies. Musculoskeletal health problems were the most frequent reason (36%) cited for an inpatient rehabilitation; arthrosis of the knees/hips (17%) and back pain (13%) are the leading pathologies cited in musculoskeletal rehabilitation. If data for the last 30 years are examined, a change in supply and demand can be observed: The number of rehabilitation stays in Austria has increased four-fold, the duration of the rehabilitation stays has decreased from four to three weeks and the most common age group (48%) includes individuals between 45–65 years of age.

1.1 Lifestyle and Physical Activity

The current literature suggests that the risk of developing chronic diseases can be minimized by up to 50% by pursuing an active lifestyle (35, 36). Almost all non-communicable diseases can be treated by therapies that include physical activity and strengthening programs (37-40). Exercise therapy, thus, has become the gold standard among medical treatments (41-44). Even small amounts of change in lifestyle and physical activity (PA) already have a positive impact on health (45-52); therefore, medical intervention programs not only aim to restore physiological functioning but also support secondary preventive goals, such as improvements in strength and aerobic capacity. The strongest effect size is evident in adults who alter their lifestyles from inactive to active (48-50). The amelioration of the physical constitution leads to health-promoting effects, such as reductions in high blood pressure due to improvements in the cardiovascular system, a better glucose profile and reductions in blood lipids (37, 53-58), but also leads to important improvements in the overall quality of life (41, 43). Physical therapy targets an increase in muscle strength and stability to minimize pain (59, 60) and maximize the range of motion. So physical activity and structured exercise are fundamental components of the process of recovery in all organ systems (9, 61-64).

1.1.1 Physical Activity and Age

Sustained physical activity in older individuals is associated with improved overall health. Significant health benefits have even been seen among participants who became physically active relatively late in life (65). On the other hand, older adults perceive age discrimination, which is associated with increased odds of poor self-rated health and an increased risk of incident serious health problems (66, 67). Elderly persons differ in how they adapt to exercise programs due to genetic and lifestyle factors (68-71). Nevertheless, physical activity promotes the aging process in that it promotes the restoration of functional capacity, particularly in elderly, sedentary persons. The acute physiological adjustments that healthy sedentary older persons need to make to perform submaximal aerobic exercise and resistance training are similar to those that young adults need to make (72-74). The introduction of exercise programs (e.g., in a rehabilitation setting) for elderly patients seems important to improve functional well-being and health care without increasing costs (75-78).

Several societies, therefore, have developed exercise therapy guidelines for the various disciplines and disease groups (53, 79-82), but there is still need to raise clinicians' awareness about the effects of exercise training as a therapy (83-85).

1.2 Rehabilitation

According to the WHO definition, the rehabilitative process can be divided into four phases: Phase I includes the early mobilization in primary treatment; phase II involves the provision of follow-up treatments or post- acute therapy in rehabilitation centers; in phase III, the long-term life-modifications are integrated and stabilized; and phase IV involves long-term rehabilitation, including mostly outpatient aftercare (Figure 1).

PHASE I	PHASE II	PHASE III	PHASE IV
acute patient care	**early patient rehabilitation**	**follow-up aftercare**	**follow-up long-term**
(acute event, primary prevention)	(post-acute care curative treatment)	(maintenance phase)	(secondary prevention)
hospital (eg. OP)	inpatient/outpatient	outpatient	outpatient
days/weeks	3-6 weeks	3-12 month	after 1 year

Figure 1: Phase model of rehabilitation.

Phase I includes the early mobilization in primary treatment; phase II involves the provision of follow-up treatments or post- acute therapy in rehabilitation centers; in phase III, long-term life-modifications are integrated and stabilized; and phase IV involves long-term rehabilitation, including mostly outpatient aftercare.

The aim of an inpatient rehabilitation [phase II (86-88)] is to restore the patient's health status based on the bio-psycho-social health model. However, rehabilitation is ideally a continuum of coordinated interventions; for this reason, beginning rehabilitation early on, and even during phase I, may be beneficial (76, 89, 90). Starting rehabilitation so early may provide an important preparation period for phase II programs. In addition, individuals who take part in short-term, center-based programs need to continue to participate in long-term outpatient programs as well commit to lifelong, self-regulated physical activity and exercise (91-93).

1.2.1 GVA – A Preventive Program

After a three-year pilot period, an inpatient secondary preventive program for patients with musculoskeletal health problems was introduced in 2018. This active health care program with a medical-secondary preventive focus [called "GVA," *Gesundheitsvorsorge Aktiv* ('Health Care Active')] replaced the classic, three-week medical spa therapy in Austria. The modular structure of the GVA places a focus on exercise based on demand (motivation and optimization) and mental health and is characterized by an increased proportion of active therapies (see Table 1). Rehabilitation and the inpatient health care program 'Health Care Active' are different in that the GVA plays a preventive role. Unlike patients in an orthopedic rehabilitation, patients in the GVA are generally younger and do not yet display disorders of the musculoskeletal system, which would require special rehabilitation treatments. The ICD classification of degenerative, inflammatory, musculoskeletal complaints is similar in both GVA and orthopedic patients, as is the chronic impairment of their functional capacity and health (2, 3). However, GVA patients have not experienced acute events, received care, or undergone recent surgical interventions (WHO Phase I; see Figure 1) on the musculoskeletal system.

1.2.2 Situation in Austria

The medical rehabilitation is structured in different ways all over the world, although a tendency toward the standardization of the social and health systems can be observed. In Germany and Austria, the social insurance system offers individuals the possibility to take part in an inpatient rehabilitation program for a period of three (up to six) weeks in specialized rehabilitation centers with an interdisciplinary team (88, 94, 95). Some other countries only provide outpatient rehabilitation. Therefore, the implementation of rehabilitation interventions varies vastly from country to country (96-102).

It has been shown that rehabilitative programs should not only include physical therapy, but also multidisciplinary interventions in the sense of behavior modifying, psychological and educational support in order to achieve maximum effectiveness (78, 103). An inpatient treatment lasts on average two to three hours per day. An individual rehabilitative program is provided, consisting of active and passive treatments (see Table 1). Active treatments consist of physical activity that includes gymnastic and individual physiotherapy sessions, and the medical training focuses on underwater, ergometer, Nordic walking, strength, balance, relaxation and motion training. Passive treatments involve sessions of massage, thermotherapy, electrotherapy and ultrasound, as well as educational lessons that include various lectures or psychological coaching. Each patient is offered a program of at least 30 hours of therapy over the three-week period, split up into approximately 50% active and 50% passive treatments; these treatments greatly surpass those listed in the physical activity guidelines of the WHO (150-minute workout with moderate intensity and strengthening exercises twice a week).

Table 1: Quantity and types of therapies offered over a three-week rehabilitation period.

The rehabilitation and GVA program consists of active and passive treatments, which last on average 2–3 hours per day. Active treatments consist of physical activity that includes gymnastic and individual physiotherapy sessions, and the medical training focuses on underwater, ergometer, Nordic walking, strength, balance, relaxation and motion training. Passive treatments involve sessions of massages, thermotherapy, electrotherapy and ultrasound, as well as educational lessons that include various lectures or psychological coaching. Each patient can take part in a program that includes a minimum of 1800 minutes of therapy over the three-week rehabilitation period (GVA: 1400 minutes), equally divided between active and passive treatments.

	Physical exercise	**Medical training**	
Active	Gymnastic	Underwater gym	Approx. 50%
	Individual physiotherapy	Ergometer training	
	Sensomotoric training	Strength training	
		Balance and function training	
		Relaxation	
	(Passive) **Treatments**	**Education**	
Passive	Massages	Health- related talks and trainings	Approx. 50%
	Thermotherapy	Psychological	
	Electrotherapy	Coaching	
	Ultrasound		
Required total amount:		At least 1800 minutes (within three weeks) [GVA at least 1400 minutes (within three weeks)]	

In Austria, diseases that are caused by inflammatory, degenerative processes, injuries, or surgeries permit an inpatient rehabilitation (WHO–Phase II) over 3–4 weeks for restoring physiological functioning and the reintegration into social and professional life. Outpatient rehabilitation is only possible in urban centers. If travel distances are too far, outpatient rehabilitation is not possible. Based on historical decisions (104) and Health Technology Assessments (HTA), there is currently a framework of contracts in place with the federal Austrian social security institutions. This includes performance agreements for rehabilitation that are based on criteria regarding the quality of processes and treatment outcomes (86). Criteria include individual, detailed results that demand a standardized statistical recording of outcome parameters from admission to up to discharge from the rehabilitation program (see Table 2). The results of the evaluation and statistical analyses of these medical outcomes are generally not open to the public (2).

Table 2: Indicators of medical quality outcomes.

Quality-of-outcome measures have to be documented in the discharge report at the beginning and the end of the phase II rehabilitation program. These quantifiable medical indicators include general health characteristics such as the patients' body measurements and cardiovascular indicators, psychological indicators such as pain and subjective health in all indications. These indicators form the unspecific outcome (UHI). Specific indicators are given for each of the different indications, such as activities of daily living (ADL; questionnaires), motor skills, or physical performance. These indicators form the indication-specific outcome (ISI). Both indices together (UHI and ISI) form the overall 'Medical Quality Outcome' (MQO_{idx}) in equal parts. UHI, ISI and MQO_{idx} were calculated for each patient, referring to the initial and discharge statuses, and the difference between these (difference: post-pre) was used as an individual success factor for rehabilitation.

Indicators for Medical Quality Outcomes (MQO_{idx}) and individual success factors (UHI, ISI)								
unspecific general health parameters			**disease-specific health parameters (indication-specific outcomes [z]; ISI)**					
MED1	BMI	[kg/m²]	quality of life	EQ-5D	[%]	walk test	6-MWT	[m]
	abdominal girth	[cm]	ergometer	Watts	[W]	quality of life	EQ-5D	[%]
	SHAPE	**[z]**	**ISI_{GVA}**	***Health through Activity (GVA)***		**ISI_{ONC}**	***Oncology Rehabilitation***	
MED2	blood pressure systolic	[mmHG]	lipids	cholesterol	[mg/dl]	quality of life	EQ-5D	[%]
	blood pressure diastolic			HDL	[mg/dl]			
	resting heart rate	[bpm]		LDL	[mg/dl]	motoric function	Roland Morris	[ ]
	CARDIOVASCULAR	**[z]**		triglycerides	[mg/dl]		WOMAC	[ ]
							Constant Murley	[ ]
MED3	VAS (pain)	[cm; 0-10]	blood glucose	HBA1C	[mmol/m]	walk test	Time up & go	[sec
	EQ VAS (self-rated health)	[%; 0-100]		blood sugar	[mg/dl]		10m	[sec
	SUBJECTIVE	**[z]**	***ISI_{MET}***	***Metabolic Rehabilitation***		**ISI_{ORT}**	***Orthopedic Rehabilitation***	
UHI	**Unspecific Health Index** MED1, MED2 & MED3	**[z]**	O_2	oxygen saturation	[%]	clin. classification	CCS / NYHA	[ ]
			respiratory function	COPD Assessment T.	[ ]	quality of life	EQ-5D	[%]
				Asthma Controll Test	[ ]	lipids	LDL, HDL, triglycerides	[mg/d
						ergometer	Watts	[W]
			walk test	6-MWT	[m]		pres. freq. prod. (DFP)	[ ]
***all indications** (ONC, MET, PUL, ORT, CAR)*			**ISI_{PUL}**	***Pulmonary Rehabilitation***		**ISI_{CAR}**	***Cardiovascular Rehab.***	

The need for primary, secondary and tertiary prevention facilities in Austria is high. For example, on the basis of the results of a representative 2014 health survey in Austria (105), the proportion of people with chronic back problems was estimated to be 24% of the population, representing 1.8 million people. Nineteen percent of all respondents complained of cervical discomfort. Osteoarthritis was found in 5% of the women and in 8% of the men. Pain symptoms experienced in the last four weeks were reported by 3.6 million individuals, with an age-related increase in prevalence and pain severity. Out of all respondents, 3.4 million persons were overweight (BMI 25.0–29.9 kg/m^2) or obese (BMI > 30 kg/m^2).

1.2.3 Effectiveness

There is strong evidence that rehabilitation is necessary as part of the treatments offered for inflammatory or degenerative diseases, as well as for post-operative conditions or injuries (106, 107). The severity of the underlying condition and the expectation that the physical function can be restored are requirements for being admitted to an inpatient rehabilitation. Physical activity programs have a positive impact (see 1.1 Lifestyle and Physical Activity). However, the dropout rate is high with respect to the maintenance of long-term activity and health-related lifestyle change. Findings support the sustained efficacy of intense, multimodal rehabilitation programs and provide moderate evidence that such programs improve subjective health status and reduce pain (108). Studies have provided a high amount of evidence for orthopedic rehabilitation, treatment after hip and knee endoprosthesis (109-112) and chronic back pain (113-115). The combination of physiological and psychological training significantly leads to positive changes (59, 116, 117). These data confirm that treatments based on a combination of physical activity and psychosocial training have an influence on pain reduction and mental well-being. This also applies to cardiovascular, lung, oncological and metabolic diseases (80, 118-125).

1.2.4 Elderly Patients

Due to the currently high life expectancies for humans, both hospital primary care facilities and secondary medical care facilities must treat a large number of old people. One challenge faced is that the functional capacity of elderly people decreases rapidly in the hospital, because the muscle strength (5% loss per day) and the capacity of endurance; (12–14% loss of VO_2 max after 10 days) significantly decreases as a result of prescribed bed rest. Studies have shown that the functional health 33% of elderly patients had regressed by the point of hospital discharge (126, 127). These findings indicate that the importance of physical exercise in a rehabilitative setting is high, as physical functionality can be improved (89). Older individuals are generally among the least fit, least active cohort; they are also at increased risk of suffering complications after an acute cardiac event and/or major surgery (128, 129) and are more susceptible than young persons to muscle loss (130). Older people have even been shown to achieve greater improvements than younger patients through exercise training and cardiac rehabilitation (67, 129, 131-133). Inpatient rehabilitation has a positive influence on the functional improvements of patients, reduces mortality and makes a significant contribution to the prevention of home care (134, 135). Even low levels of physical activity have been shown to produce significant improvements, such as a 22% reduction in mortality (42, 136).

1.2.5 Sustainability

To successfully recover from a disease after rehabilitation, the patient's healing process must have a certain continuity. For this reason, rehabilitative programs also place a focus on sustainability, such as engaging in a sufficient amount of physical activity after the rehabilitation. Therefore, an inpatient stay should also lead to a health-related modification in lifestyle. Studies show that about 57% patients in Europe and even 70% patients in the US are able to return to their regular, full-time jobs and show significant improvements in psychosocial, physiological parameters after participating in an inpatient rehabilitation (137-

140). After taking part in an interdisciplinary treatment program that includes medical, physical-activity-based and psychological therapy, the number of individuals who re-enter the job market remains high (141, 142). During the rehabilitative stay, pain can be significantly reduced, and long-term improvements in physiological functionality can be achieved. The success can be measured even up to 12–21 months after rehabilitation (106, 143, 144).

Long-lasting effects of rehabilitation or spa therapy, respectively, may be due to new habits in terms of adaptation physiology, recreational effects (145) and changes in lifestyle. Series of therapeutic stimuli experienced over a defined period lead to functional adaptations; these, in turn, are characterized by improvements in regulatory qualities and the economization and normalization of physiological functions (146). Therefore, multidisciplinary inpatient rehabilitation programs are much more effective than a simple outpatient therapy program performed with a physical therapist. In contrast, programs performed at a health care center are usually intensive. It is still unclear whether some kind of periodization, including recovery phases for the physical training, needs to be included in such programs. In addition, if the direct effect of the program is evaluated after three to four weeks, patients may be fatigued due to the intensive program and need at least three to four days to recover and see the effects of the program.

1.2.6 Quality Criteria

The structure of the inpatient rehabilitation unit is an important feature for the quality of care. The definition of standards and appropriate offers of therapy and treatments allow the patients to achieve better health (see Table 1). Clinical standards for rehabilitation recommend the routine collection of standardized outcome measures (see Table 2), which can be used to evaluate the impact of rehabilitation and allow the comparison of different populations, programs and practices (147).

Medical outcome quality is defined as the „*measurable change in the professionally assessed state of health, the quality of life and the satisfaction of a patient*" [see Austrian Federal Quality of Healthcare Act, GQG (148)]. The outcomes become visible by "*the difference between the initial state and the state at treatment end*" (149).

Outcome measurement in rehabilitation can be based on various methodological approaches, such as questionnaires, performance tests, equipment measurements and functional physical examinations. The outcome quality measurement, “the outcome,” includes features on health (e.g., symptoms, pain), functional levels (e.g., performance) and educational levels. In addition to the patient's subjective assessment, ("Patient-Reported Outcomes"), health care professionals document medical, diagnostic and other relevant outcome measures or criteria [e.g., International Classification of Functioning, Disability and Health (ICF)].

Outcome assessments are widely used in routine clinical rehabilitation and health care, but current and published results of multiple medical outcomes with individual patient data for inpatient health care programs are not available (150).

1.3 Objectives and Questions

It is becoming increasingly important to justify the medical effectiveness of rehabilitation for practical and health care reasons. Constantly changing framework conditions present challenges for quality assurance management, in which structural, process and outcome characteristics are used to evaluate the degree to which predefined goals have been achieved.

Despite mandatory requirements, standardization and high-quality standards, routine medical results are rarely used and processed in practice. The technical means to do so have existed for decades, and a continuous, automated evaluation is only a question of definition and coordination. Some individual efforts and registers have been made, e.g., for cardiac rehabilitation of phase III (151). The level of competence of the individual institutions, experts and specialist societies is high. However, routine results on rehabilitation in Austria are not open to the public and not transparently available to health professionals and patients. Ideally, the Austrian social insurance institutions would make these results available, as they determine and check the structures, processes and contents of health care. Current performance profiles[3] are not publicly accessible and are not explained and justified in more detail using evidence-based sources. A clear and proven form and structure is determined without continuously observing the consequences of this content and the framework. In this way, a doctor/therapist can only assess his or her expectations and the assessment of a successful treatment based on his or her personal experience and knowledge.

As a sole use of "primary patient-oriented" assessments to assure the quality of outcomes, the subjective assessment and satisfaction through self-reporting of patients may not be sufficient for the valid evaluation of medical success, impact and sustainability. The length of stay and complications, as well as quality registers on surgical frequencies, do not make clear statements about the expected medical and health success of the treatment. Therefore, reference values for unspecific general health and a disease-specific medical

[3] Note: In addition to the undisputed advantages (e.g. quality and safety) of performance profiles, these can also have disadvantages with regard to new promising medical developments, personalized treatments or the strengthening and motivation of health professionals.

indicator that are extracted from routine measurements would be important and valuable additions to the medical outcome quality evaluation. These can contribute to the design processes and further developments of quality assurance in rehabilitation facilities. However, publications on this topic are rare, and current data on the medical routine outcomes of rehabilitation in Austria are unavailable.

The aim of this dissertation work was to make elementary clinical reference data available and show expected changes relating to an inpatient rehabilitation. We provide a valid basis for routinely assessed medical quality outcomes that are based on common and obligatory data acquisition. The focus, therefore, was placed on general (unspecific) and indication-specific medical indicators. The continuous collection of medical reference values has diverse potential benefits, including increasing quality assurance, raising awareness and supporting goal setting, decision-making and evaluation processes in different care models.

1.3.1 Derived Questions

On the basis of information extracted from the literature and our personal experiences, we formulated the following hypotheses:

a. The majority of the patients improve from the time of their admission up until their discharge from their inpatient health care stay.
b. Patient characteristics, such as sex, age, BMI and pre-treatment physical activity (PA), have significant impacts on their medical initial status, but not on the overall observed health care outcome.
c. Improvements in unspecific vs. indication-specific outcome indicators are of comparable magnitude.
d. Unspecific vs. disease- (indication-)specific outcomes are not directly (linearly) related to each other.
e. Initial values and timing of post-acute rehabilitation play important roles, in particular for disease-specific health changes.
f. Stratification characteristics of patients have no significant impact on the observed rehabilitation outcome. Inpatient rehabilitation works for nearly everybody.

2. Materials and Methods

In this work, we provide clinical reference data related to an inpatient rehabilitation and present how they dynamically and temporally change. A pre-post design was used in this work to perform monocentric routine outcome measurements in inpatient health care. The medical quality outcome parameters, which were previously established in the performance profile of the Austrian Social Security Institutions, served as the basis for this work (86). Descriptive, standardized, numeric medical indicators as well as monocentric reference data for a three-week inpatient rehabilitation and GVA were provided. Physicians and health care professionals performed the data collection during routine medical treatments. The standardized clinical characteristics of patients were recorded systematically at the points of admission and discharge (see Table 2). These “quality-of-outcome” measures were documented in the discharge report at the beginning and at the end of the health care program. As a result of this research, a simple evaluation model is provided in which independent factors were used to carry out a simplified evaluation of the outcome quality (2).

Table 3: Factor formation for unspecific health outcomes.

Unspecific effects of an inpatient health care stay were calculated based on monocentric normative data from the study center, including all patients who underwent a three- to four-week inpatient medical rehabilitation or GVA. The selection of clinical parameters complies with the requirements of Main Association of Austrian Social Security Institutions in the performance profiles of accredited Austrian institutions with regard to the quality of results, which should guarantee comparable medical service quality standards. The Unspecific Health Index (UHI) was calculated by summarizing the clinical data for all patients from different indications.

Results of PCA

PCA, Varimax with data of admission and discharge (60844 measurements, 33501 patients)

Factor	Variable	Communality	Loading (rotated)	% VAR	Beta-coefficient	Regression
MED 1 [*z*]: SHAPE	**BMI** [kg/m^2]	.931	.958	32.259	.516	MED1 = -6.249 + BMI * 0.095 + WC * 0.036
	WC [cm]	.933	.957		.509	*R* = 0.991
MED 2 [*z*]: CARDIO-VASCULAR	**RR_{sys}** [mmHg]	.737	.857	18.811	.517	MED2 = -11.730 + RR_{dia} * 0.069 + RR_{sys} * 0.040 + RP * 0.017
	RR_{dia} [mmHg]	.752	.842		.551	
	RP [bpm]	.141	.327		.210	*R* = 0.988
MED 3 [*z*]: SUBJECTIVE	**VAS** [cm; 0–10]	.640	.799	17.165	.614	MED3 = 1.723 + VAS * 0.255 + EQ-VAS * -0.035
	EQ-VAS [%; 0–100]	.642	-.795		-.607	*R* = 0.987
Unspecific Health Index	**UHI**	**mean MED1, MED2 and MED3**			three factors	**68.24% VAR**

WC: waist circumference; RRsys/dia: blood pressure systolic/diastolic; RP: resting heart rate; VAS: Visual Analogue Scale (Pain; 0–10); EQ-VAS: self-rated health (0–100); high (positive) values [z] correspond to worse expression.

*PCA with 68.24% explained variance (VAR); MED1: 32.26%, MED2: 18.81%, MED3: 17.17%. Unspecific health outcomes make up three factors, which were averaged to obtain an overall result, the "Unspecific Health Index (UHI)". No multiple loadings were made on other factors. The factor structure is stable in terms of content and time: PCA at admission, discharge, or difference values (discharge vs. admission) or factor solutions within one-indication show similar results. *. Retest reliability:* $r_{MED1} = .985$, $r_{MED2} = .320$, $r_{MED3} = .678$, $r_{UHi} = .731$;

The data were summarized by performing descriptive evaluations, i.e., content and factor analyses (see Table 3 and 2.2.1 Quantifying 'Medical Quality Outcome, p. 25), respectively. Below, an example is given of how to calculate the Unspecific Health Factor (UHI) for a healthy person …

… with a BMI of 22 kg/m^2, a waist circumference of 85 cm, a resting blood pressure of 119/79 mmHg, a resting heart rate of 70 bpm, a VAS (pain score) of 0.5 and a self-rated health of 95% (EQ-VAS), which leads to a result of MED1 = -1.10, MED2 = -0.33, MED3 = -1.47 and an UHI = -0.97; so, a z-score around -1 for healthy people.

2.1 Total Sample at the Clinical Trial Center

During the study period of 2016–2018, 16,966 rehabilitation patients with different medical indications (61.52 ± 12.51 years, 46.4% women; Figure 2, Table 4) were enrolled in a specialized interdisciplinary hospital for rehabilitation (clinical trial center: Humanomed Center Althofen). For GVA, data from 7,448 patients with different medical diagnoses (48.99 ± 6.15 years, 53.7% women; Table 4, below) were collected . Further data from specific individual clinical samples are presented in the results section (1, 4). In total, routine data from 24,414 patients with different medical diagnoses (57.9 ± 12.4 years, 48.5% women) were statistically analyzed. Thirty-seven percent of these patients were older than 61+ years.

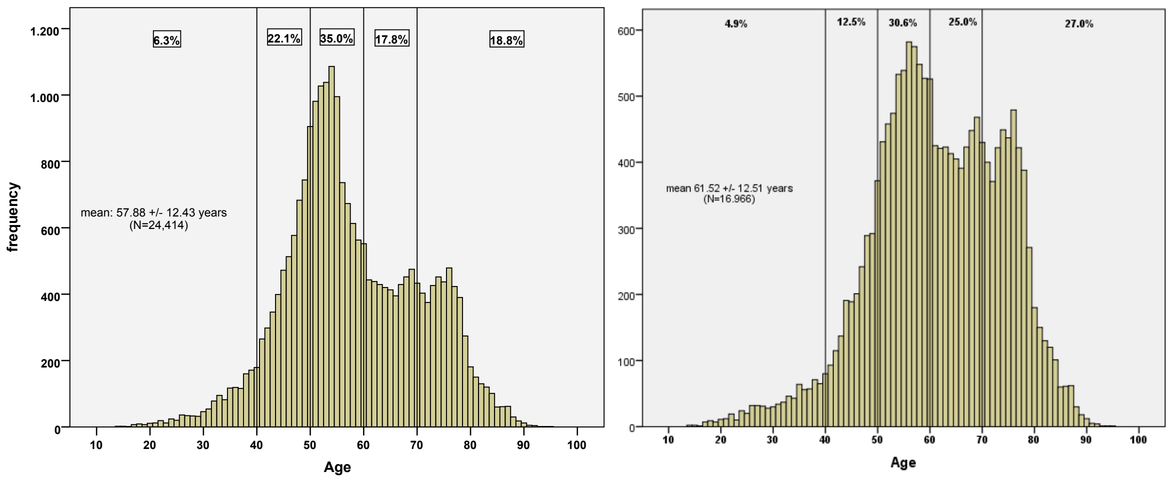

Figure 2: Age distribution of the total sample (left) and the rehab sample (right).

The number of patients with chronic diseases who participated in inpatient rehabilitation in the study center increases significantly over the age of 40. There are three age peaks near 60, 70 and 80 years of age.

The average inpatient rehabilitation length of stay was 20.98 ± 3.5 days, and 3.7 percent of all patients discontinued their inpatient treatment prematurely due to a loss of rehabilitation capacity, acute illness, or for private reasons (criterion < 18 days). Early dropouts did not depend on sex (p = .859), but there was a correlation with age, such as older patients had a higher dropout risk (p < .01). Smallest dropout quotes could be observed for orthopedic patients (2.2%), highest for metabolic patients (8.2%; p < .01). There were also weak correlations between dropout risk and initial values, but dropouts had a worse health status at admission (CI for mean z-difference: [-0.28, -0.17]; $p < .01$). In 17.3% of the patients, the inpatient stay was four weeks.

The average length of the 'Health Care Active' program (GVA) was 21.73 ± 1.85 days (incl. dropouts). Of all patients, 1.9% prematurely discontinued their inpatient treatment due to a loss of health capacity (e.g., acute illness) or for private reasons (criterion < 18 days). A categorization of the reasons for hospital treatments was based on the admission diagnosis. Almost every patient suffered from several chronic diseases, such as obesity, hypertension, or another musculoskeletal or metabolic disease. The most frequent and main diagnosis was dorsalgia (M54; 86.6% of patients with a main diagnosis of the back / spine).

Table 4: Total sample - number of patients by indication, age and sex.

Tab. 4a. The rehab sample included 18,398 patients; the analytical sample consisted of 16,966 patients (92.2%) who attended the rehabilitation program for at least 17 days and for whom valid measurements for admission and discharge were available. In the rehab sample, 4.1% of patients had missing values, and 3.7% discontinued their inpatient treatment prematurely.

Tab. 4b. The GVA sample included 7,765 patients; the analysis sample consisted of 7,488 patients (95.9%) who had accrued more than 17 days of a health care stay and valid measurements for admission and discharge. From a total GVA sample, 167 patients (2.1%) had missing values and 150 patients (1.9%) prematurely discontinued their inpatient treatment (dropouts). Early dropouts vs. planned discharge from clinic: Dropouts depended neither on sex (p = .564) nor on age (p = .702). No correlations were found between dropout risk and initial values (p > .38).

absolute (no.) and relative (%) frequency		age [years]		<= 40		41–50		51–60		61–70		71+		total	
		mean	SD	no.	%	no.	%	no.	%	no.	%	no.	%	no.	%
Orthopedic	female	62.82	13.40	216	4.9%	548	12.4%	1195	27.1%	968	21.9%	1489	33.7%	4416	51.8%
50.2%	male	59.00	13.42	350	8.5%	632	15.4%	1326	32.3%	906	22.1%	893	21.7%	4107	48.2%
	total	**60.98**	**13.54**	**566**	**6.6%**	**1180**	**13.8%**	**2521**	**29.6%**	**1874**	**22.0%**	**2382**	**27.9%**	**8523**	**100.0%**
Cardiovascular	female	66.57	11.66	18	1.7%	75	7.3%	224	21.7%	253	24.5%	461	44.7%	1031	28.4%
21.4%	male	62.82	11.38	72	2.8%	255	9.8%	804	30.9%	724	27.8%	749	28.8%	2604	71.6%
	total	**63.88**	**11.58**	**90**	**2.5%**	**330**	**9.1%**	**1028**	**28.3%**	**977**	**26.9%**	**1210**	**33.3%**	**3635**	**100.0%**
Metabolic	female	57.68	10.70	16	6.1%	39	14.9%	106	40.6%	66	25.3%	34	13.0%	261	36.5%
4.2%	male	56.69	9.73	20	4.4%	89	19.6%	191	42.1%	120	26.4%	34	7.5%	454	63.5%
	total	**57.05**	**10.10**	**36**	**5.0%**	**128**	**17.9%**	**297**	**41.5%**	**186**	**26.0%**	**68**	**9.5%**	**715**	**100.0%**
Oncology	female	59.24	11.48	57	4.1%	245	17.6%	499	35.8%	326	23.4%	266	19.1%	1393	64.2%
12.8%	male	59.83	11.45	46	5.9%	97	12.5%	276	35.5%	208	26.8%	150	19.3%	777	35.8%
	total	**59.45**	**11.47**	**103**	**4.7%**	**342**	**15.8%**	**775**	**35.7%**	**534**	**24.6%**	**416**	**19.2%**	**2170**	**100.0%**
Pulmonary	female	63.07	10.16	12	1.6%	67	8.7%	238	30.9%	257	33.4%	196	25.5%	770	40.0%
11.3%	male	63.64	9.98	23	2.0%	74	6.4%	334	29.0%	419	36.3%	303	26.3%	1153	60.0%
	total	**63.41**	**10.06**	**35**	**1.8%**	**141**	**7.3%**	**572**	**29.7%**	**676**	**35.2%**	**499**	**25.9%**	**1923**	**100.0%**
overall (Rehab.)	female	62.53	12.67	319	4.1%	974	12.4%	2262	28.7%	1870	23.8%	2446	31.1%	7871	46.4%
100.0%	male	60.64	12.31	511	5.6%	1147	12.6%	2931	32.2%	2377	26.1%	2129	23.4%	9095	53.6%
	total	**61.52**	**12.51**	**830**	**4.9%**	**2121**	**12.5%**	**5193**	**30.6%**	**4247**	**25.0%**	**4575**	**27.0%**	**16966**	**100.0%**

Influence of age on: Indication: $\eta_p^2 = .023$, Sex: $\eta_p^2 = .002$, Indication x Sex: $\eta_p^2 = .006$;

	mean	SD	<= 40	41–50	51–60	61–70	71+	total	
total sample (Rehab. & GVA)	**57.88**	**12.43**	6.3%	22.1%	35.0%	17.8%	18.8%	**24.414**	**48.5% female**

absolute (no.) and relative (%) frequency		age [years]		<= 40		41–50		51–60		61–70		71+		total	
		mean	SD	no.	%	no.	%	no.	%	no.	%	no.	%	no.	%
GVA	female	49.26	5.74	307	4.1%	1786	24.0%	1867	25.1%	33	0.4%	10	0.1%	4003	53.7%
28.9%	male	48.68	6.58	392	5.3%	1498	20.1%	1484	19.9%	57	0.8%	14	0.2%	3445	46.3%
	total	**48.99**	**6.15**	**699**	**9.4%**	**3284**	**44.1%**	**3351**	**45.0%**	**90**	**1.2%**	**24**	**0.3%**	**7448**	**100.0%**

Reasons for inpatient rehabilitation were based on the admission diagnosis. The most frequent diagnoses cited at the study center were chronic ischemic heart disease, osteoarthritis of the knee and hip, chronic obstructive pulmonary disease, dorsalgia and malignant neoplasm of the breast (see Table 5). Categorizations are based on ICD-10 at admission and are dependent on age (diagnosis explained by age: $\eta_p^2 = 0.144$) and related to the number of additional diagnoses ($\eta_p^2 = 0.382$). Orthopedic patients with fractures of the femur (S72), spondylopathies (M48) and osteoarthritis of the knee and hip were older, as well as patients with nonrheumatic aortic valve disorders (I35), interstitial pulmonary diseases (J84) and malignant neoplasm of the bladder (C67). Younger patients were more frequently diagnosed with dorsalgia and disc disorders, asthma and malignant neoplasm of the breast. Metabolic patients had an especially high number of additional diagnoses, as did orthopedic patients with fractures. Sex played a minor role regarding the types of diagnoses ($\eta_p^2 < .01$), with the exception of the oncological area and for J84, I25 and I48.

Table 5: Frequent ICD diagnoses in the rehab sample.
Categorizations were based on ICD-10 at admission and are dependent on age.

IND	ICD	Most frequent diagnoses (ICD-10)	N	age	female
Orthopedic	M17	Osteoarthritis of knee	1584	66.75 ± 10.50	55.9%
	M16	Osteoarthritis of hip	1359	67.03 ± 11.00	53.9%
	M54	Dorsalgia	1087	57.13 ± 12.53	50.3%
	M51	Thoracic, tl., and ls. lv. disc disorders	724	53.29 ± 12.83	44.6%
	M75	Shoulder lesions	711	58.24 ± 9.65	43.3%
	S72	Fracture of femur	277	70.71 ± 13.10	66.8%
	S82	Fracture of lower leg, including ankle	276	54.77 ± 14.35	52.9%
	M19	Other and unspecified osteoarthritis	275	64.79 ± 12.31	56.4%
	M48	Other spondylopathies	261	69.07 ± 10.50	49.4%
Cardiovascular	I25	Chronic ischemic heart disease	2397	64.04 ± 10.75	23.8%
	I35	Nonrheumatic aortic valve disorders	319	68.62 ± 12.43	39.8%
	I42	Cardiomyopathy	142	59.85 ± 11.92	30.3%
	I48	Atrial fibrillation and flutter	119	66.51 ± 10.79	37,0%
	I10	Essential (primary) hypertension	87	59.40 ± 10.31	36.8%
Pulmonary	J44	Other chronic obstructive pulmonary disease	1194	64.92 ± 8.54	37.3%
	J45	Asthma	272	58.44 ± 11.52	53.7%
	I26	Pulmonary embolism	67	60.64 ± 12.43	43.3%
	J84	Other interstitial pulmonary diseases	66	70.47 ± 8.86	18.2%
Metabolic	E11	Type 2 diabetes mellitus	251	59.82 ± 8.98	35.1%
	E66	Overweight and obesity	217	54.21 ± 9.85	41.0%
	E14	Unspecified diabetes mellitus	126	59.78 ± 9.74	32.5%
	E10	Type 1 diabetes mellitus	47	49.47 ± 12.77	55.3%
Oncology	C50	Malignant neoplasm of breast	731	57.97 ± 11.42	98.5%
	C34	Malignant neoplasm of bronchus and lung	170	62.82 ± 8.38	49.4%
	C61	Malignant neoplasm of prostate	167	63.28 ± 8.34	0.00%
	C18	Malignant neoplasm of colon	115	60.32 ± 11.88	51.3%
	C20	Malignant neoplasm of rectum	77	63.01 ± 10.56	37.7%
	C85	Other types of non-Hodgkin lymphoma	58	61.38 ± 13.21	55.2%
	C56	Malignant neoplasm of ovary	58	59.40 ± 10.46	100.0%
	C16	Malignant neoplasm of stomach	56	62.30 ± 11.75	51.8%
	C67	Malignant neoplasm of bladder	45	67.49 ± 8.22	26.7%
	C25	Malignant neoplasm of pancreas	44	65.66 ± 10.99	68.2%
total		*(78.86% of sample)*	13379	62.56 ± 11.92	46.0%

Influence of Age: ICD: $\eta_p^2 = .144$ Sex: $\eta_p^2 = .004$, Sex x ICD: $\eta_p^2 = .007$; Number (no.) of diagnoses: ICD: $\eta_p^2 = .382$, on Sex: $\eta_p^2 = .000$, Sex x ICD: $\eta_p^2 = .005$; No. of diagnoses female 1.56 ± 0.72, male 1.53 ± 0.79;

The period between acute care (surgery, chemotherapy) and rehabilitation was 13.8 ± 24.2 weeks (see Table 6). However, orthopedic patients with surgery of knee, hip, or shoulder and cardiovascular patients with chronic ischemic heart disease and nonrheumatic aortic valve disorders progressed earlier from phase I to phase II (10.7 ± 18.4 weeks). For these patients, a quasi-experimental control group results from the different onset times, the period between acute care and the start of the follow-up treatment procedure (inpatient rehabilitation phase II).

Table 6: Admission of rehabilitation and time between surgery and ICD-diagnoses.

Orthopedic patients who had undergone knee, hip, or shoulder surgery and cardiovascular patients with chronic ischemic heart disease and nonrheumatic aortic valve disorders progressed from phase I to phase II within 10.7 ± 18.4 weeks on average. This subsample of patients formed a quasi-experimental waiting group via different onsets for inpatient rehabilitation.

	ICD and patients with surgery (OP) (cf. Table A1)		Post-OP time: time from OP to rehabilitation phase II [days]						OP	total no.
			<= 42 (6 weeks)	43–70	71–105	106–366	> 1 year	mean ± SD		% with OP
Orthopedic	**M17**	no.	661	391	253	152	16	66.42 ± 105.82	1473	1584
	Osteoarthritis of knee	%	44.9%	26.5%	17.2%	10.3%	1.1%		20.7%	93.0%
	M16	no.	533	403	199	124	23	67.43 ± 111.80	1282	1359
	Osteoarthritis of hip	%	41.6%	31.4%	15.5%	9.7%	1.8%		18.0%	94.3%
	M54	no.	14	37	59	85	26	203.93 ± 366.27	221	1087
	Dorsalgia	%	6.3%	16.7%	26.7%	38.5%	11.8%		3.1%	20.3%
	M51	no.	23	97	103	141	19	136.86 ± 247.66	383	724
	Thoracic, tl., and ls. lv. disc disorders	%	6.0%	25.3%	26.9%	36.8%	5.0%		5.4%	52.9%
	M75	no.	165	195	105	134	16	91.93 ± 133.98	615	711
	Shoulder lesions	%	26.8%	31.7%	17.1%	21.8%	2.6%		8.6%	86.5%
	S72	no.	47	80	68	62	10	102.10 ± 114.07	267	277
	Fracture of femur	%	17.6%	30.0%	25.5%	23.2%	3.7%		3.8%	96.4%
	S82	no.	7	39	86	96	10	149.23 ± 200.95	238	276
	Fracture of lower leg, including ankle	%	2.9%	16.4%	36.1%	40.3%	4.2%		3.3%	86.2%
	M19	no.	46	75	52	45	9	122.60 ± 298.95	227	275
	Other and unspecified osteoarthritis	%	20.3%	33.0%	22.9%	19.8%	4.0%		3.2%	82.5%
	M48	no.	15	34	81	82	8	119.91 ± 103.65	220	261
	Other spondylopathies	%	6.8%	15.5%	36.8%	37.3%	3.6%		3.1%	84.3%
Cardiovascular	**I25**	no.	731	273	306	468	29	85.61 ± 153.62	1807	2397
	Chronic ischemic heart disease	%	40.5%	15.1%	16.9%	25.9%	1.6%		25.4%	75.4%
	I35	no.	187	28	27	32	2	50.57 ± 114.0	276	319
	Nonrheumatic aortic valve disorders	%	67.8%	10.1%	9.8%	11.6%	0.7%		3.9%	86.5%
	I42	no.	6	11	15	25	1	119.10 ± 77.60	58	142
	Cardiomyopathy	%	10.3%	19.0%	25.9%	43.1%	1.7%		0.8%	40.8%
	I48	no.	9	5	12	9	0	95.17 ± 75.17	35	119
	Atrial fibrillation and flutter	%	25.7%	14.3%	34.3%	25.7%	0.0%		0.5%	29.4%
OP (41.9% of sample)		no.	2444	1668	1366	1455	169	89.34 ± 161.64	7102	9531
orthopedic & cardiac diagnoses		%	34.4%	23.5%	19.2%	20.5%	2.4%		100.0%	74.5%

2.1.1 Ethical aspects

This research (Routine Outcome Parameters of an Inpatient Rehabilitation in Austria) was reviewed and approved by an Ethics Committee (Vote by the Ethics Committee of the Medical University of Graz, dated 02.05.2019, EC Protocol Number: 31-321 ex 18/19). Person-related and health-related data were collected as part of routine medical care and quality management performed at the Humanomed Center Althofen (9330 Althofen, Moorweg 30). Data processing was done by following a standard operating procedure by the responsible data processing party: Humanomed Center Althofen GmbH, Data Protection Officer: Mag. Karl Klein, Jesserniggstraße 9, 9020 Klagenfurt. Individual patient data from the hospital information system were compiled in compliance with all regulations of the Austrian Privacy Act and the Declaration of Helsinki in the currently valid version. The data were collected in accordance with national legislation (e.g., hospital laws, contracts with insurable institutions) with the aim of collecting mainly scientific data in the interest of the public.

Studies with non-routine specific measurements or treatments were authorized by the Ethical committee of the Carinthian government with authorization number A 02/05 (4) and A11/14 [(1), BASG-No.: INS-621000-0655, EUDAMED-Ref.no.: CIV-AT-15-02-013172].

2.2 Medical Outcome Quality

Outcome measurements in rehabilitation were performed by taking various methodological approaches, such as issuing questionnaires, conducting performance tests, collecting measurements with equipment and carrying out functional physical examinations (see 1.2.6 Quality Criteria, p. 17). The aim of the present work is to provide a valid basis for routinely assessing the quality of medical outcomes based on common data acquisition (routine outcome measurement). The focus was placed on general (unspecific, body-constitution-based) and indication-specific parameters (see Table 2).

2.2.1 Quantifying 'Medical Quality Outcome'

In addition to the descriptive analysis of individual medical parameters (Table 2), the effects of inpatient rehabilitation were evaluated based on aggregated medical quality factors (e.g. Table 3). These were calculated using monocentric normative data from the study center (cf. Figure 3), including all available patients (period from 2016–2018) who underwent a three- to four-week inpatient medical rehabilitation. The selection of clinical parameters followed the requirements of Main Association of Austrian Social Security Organizations in the performance profiles of accredited Austrian institutions on the quality of results, which should guarantee a comparable medical service quality standards. Success factors, such as an unspecific health index for all patients with different indications and a specific index within each indication, were formed by summarizing the compulsory clinical data (2, 3).

i. The 'Unspecific Health Index' (UHI) is the arithmetic mean of three independent areas of measurements: body measurements ('shape'; BMI and abdominal circumference), 'cardiovascular' indicators (blood pressure and resting heart rate), 'subjective' discomfort (visual analogue scales (VAS pain, 152) and subjective health status (EQ-VAS, 153). These indicators are believed provide a simple and quick overview of the 'unspecific' aspects that influence the effectiveness of a rehabilitation or health care stay (see Table 3).

ii. The 'Indication Specific Index' (ISI) corresponds to the *z*-normalized means of homogeneous medical content areas such as daily activities, motor skills, or physical performance for each indication (see following '2.2.2 Statistical Methods').

iii. Both indices together form the overall "Medical Quality Outcome" (MQO_{idx}) in equal parts (see Table 2).

The Unspecific Health Index (UHI) can be interpreted as an indicator of general health status or the current body constitution, whereas the Indication Specific Index (ISI) corresponds to a more disease-specific health indicator. Both indices together form the overall "Medical Quality Outcome" (MQO_{idx}).

2.2.2 Statistical Methods

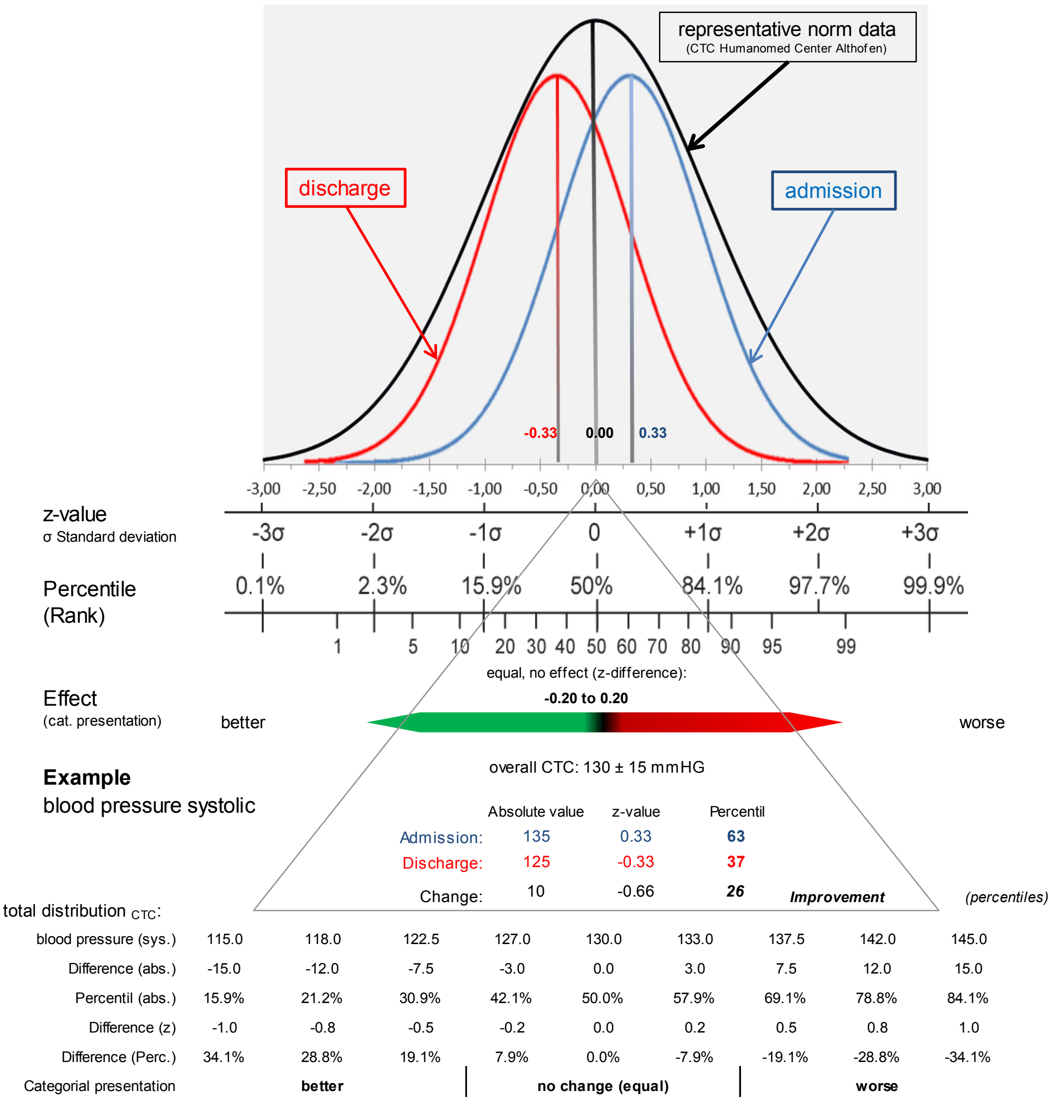

Figure 3: Explanation of the methodology: distribution, effect sizes and percentiles.

Outcome parameters can be transformed into z-values, which allow a conversion into percentiles. By means of the z-standardization, differently scaled quantities were summarized and changes were uniformly quantified.

Based on the value distributions, the individual outcome parameters were transformed into *z*-values, which allowed a conversion into percentiles. By means of *z*-standardization, differently scaled quantities were summarized, and the changes were uniformly quantified. A value of 50% (median) or a *z*-value of zero corresponded to the representative mean of the admission and discharge data for all patients at the clinical trial center. Difference-values with no significant changes normally range randomly from 0.00 ± 0.20 (see Figure 3). Changes between admission to discharge were revealed by examining the effect sizes and the number of patients (relative frequencies), which could be improved in clinically relevant ways (categorical presentation: better, equal, worse). The threshold used was an average *z*-difference of > 0.20 for unspecific general health parameters and for disease-specific parameters. For aggregated factors like the Unspecific Health Index (UHI), Specific Index (ISI) and overall Medical Quality Outcome (MQO_{idx}), the threshold is around > 0.33 (SMD). A larger positive *z*-value or a negative percentile corresponds to a below-average (worse) value in the sample. Negative *z*-differences generally correspond to an improvement.

Statistical data processing was performed using IBM® SPSS® Statistics (version 22) software. The statistical analysis included parametric methods such as multifactorial variance analyses for repeated measurements and the calculation of Pearson correlations. Individual missing values were not replaced for the per-protocol analysis. The specification of *p*-values is only specified in borderline cases (if not explicitly stated: $p < .001$), and effect sizes were used instead (partial Eta² (η_p^2) and *z*-standardized mean differences). The representation of the η_p^2 was chosen because very small numerical differences became statistically significant even if they were not relevant in terms of content and clinical relevance. An η_p^2 that ranges from .01–.06 corresponds to a small effect. Ranges of .06–.14 correspond to a middle effect, and values > .14, to a large effect.

3. Collections of Papers on Inpatient Rehabilitation: Results

This chapter presents the results of this cumulative dissertation work and provides a detailed overview of the main topics that were extracted from a literature review of papers on inpatient rehabilitation. In this chapter, after the citation is stated, each paper is summarized and insight is given on its content, research method and results. Some of these original contributions are open access contributions (3-5); otherwise, they are linked in the Appendix 2 (see 6.3 Original Contributions, p.71) as accepted author's version of the original research article (1, 2).

3.1 Overview

The aim of providing this overview is to present elementary clinical reference data that are useful for health care professionals and patients. We show what can be expected from inpatient rehabilitation in Austria. The collection of papers provides a valid basis for routinely assessed medical quality outcomes based on common and obligatory data acquisition. In this way, a standardized use of routine outcome measures supports quality assurance and an evaluation of different treatment pathways or new therapeutic possibilities.

In the first paper, we introduce a simple model of independent factors that can be used to perform an aggregated evaluation of the unspecific medical quality outcome. In a second work, these unspecific health factors are expanded to include disease-specific indicators. In addition to these basic medical indicators, additional promising physiological areas are identified, such as cardiac autonomic control, assessed via heart rate variability (HRV). In this context, we show the dynamic changes that occur over time due to inpatient rehabilitation and the impact of single therapy applications in further work. Important influencing factors, like lifestyle and physical activity for inpatient health care are presented at the end of this section.

3.2 Medical Quality Outcomes - Routine Outcome Measures

3.2.1 Unspecific Outcome Parameters of an Inpatient Rehabilitation

Table 7: Bibliographic information of paper '2' - Unspecific Outcome Parameters.

Title Medical Quality Outcomes: Unspecific Outcome Parameters of an Inpatient Musculoskeletal System Rehabilitation in Austria - Monocentric clinical reference values of a descriptive evaluation model for routine outcome measurements in Orthopaedic Rehabilitation and the "Health through Activity" programme
Citation (2) Grote, V., Böttcher, E., Mur, E., Kullich, W., Puff, H. (2019). Medical Quality Outcomes: Unspecific Outcome Parameters of an Inpatient Musculoskeletal System Rehabilitation in Austria. Phys Med Rehab Kuror, 29(02), 104-117. doi:10.1055/a-0835-6481
Abstract **Purpose:** As part of the documentation for all patients who benefit from inpatient rehabilitation, standardized collection of data relating to performance indicators for medical quality outcomes (MQO) is obligatory. Publications on this subject, however, are rare. The aim is to make available elementary clinical reference data and show changes relating to an inpatient musculoskeletal rehabilitation. **Materials and Methods:** The outcome parameters required by funding agencies in the service profile include, besides disease-specific parameters, unspecific general health parameters such as body measurements, circulatory parameters and health problems. Data from 11 414 patients (54.7 ± 12.3 years, range: 14–95; 53% women) who had undergone orthopedic rehabilitation or a "Health through Activity" programme, were statistically analysed. **Results:** Unspecific MQO indicators can be summarized in three categories (explained variance 71%). There is variation in the initial values according to indication and gender. The effect of inpatient rehabilitation stay is comparable. 74% of patients gain immediate benefit from the rehabilitation. 20% of patients show no change and 6% get worse. In contrast to circulatory parameters and symptoms, anatomical characteristics remain practically unchanged. **Discussion and Conclusions:** Inpatient rehabilitation setting reduces risk factors in the majority of patients and improves general well-being, although not all those having rehabilitation reach such a level of success. In order to improve the success rate and sustainability of the treatment, differentiation of treatment pathways is required. In this way, clinical reference values can provide a valuable contribution to quality assurance and evaluation.
Keywords Inpatient rehabilitation, medical quality outcomes, routine outcome measurement, reference data;
Contribution to the dissertation and hypotheses Based on basic data acquisition in inpatient rehabilitation, we introduce a simple model of independent factors for an aggregated assessment of the unspecific health outcome. We show that the majority of the patients improve from the time of their admission up until their discharge from their inpatient health care stay and patient characteristics, such as sex and age have significant impacts on their medical initial status, but not on the overall observed health care outcome (cf. 1.3.1 Derived Questions, p.19).
Special features, notes Routine data from 11,414 patients who had undergone orthopedic rehabilitation or a GVA program between February 2016 and April 2018.

A comparison of unspecific health factors with new and old data (see Table 3 vs. Table 8) underlines the stability of the factor structure and the validity of the results. In addition to presenting unspecific results and clinical reference values of inpatient rehabilitation, this paper (2) contains perspectives on further relevant topics. Issues are addressed such as sex and age differences, the influence of the time of entry on the rehabilitation and the relationship between disease-specific and unspecific medical parameters.

Table 8: Factor formation for orthopedic and GVA patients.
Unspecific health factors of an inpatient health care stay were calculated based on monocentric normative data received from the study center, including only orthopedic and GVA patients.

Principal Component Analysis - Calibration sample: Patients from orthopedic rehabilitation and GVA
PCA, Varimax with data of admission and discharge (22,789 measurements in 11,414 patients)

Factor	**Parameter**	**Communality**	**Loading** (rotated)	**% VAR**	**Beta-coefficient**	**Regression**
MED 1 [z]: **SHAPE** *[Anatomische Merkmale]*	**BMI** [kg/m²]	0.933	0.958		0.520	MED1 = -6.583 + BMI * 0.100 + WC * 0.038
	WC [cm]	0.934	0.955	**33.23**	0.503	R = 0.989
MED 2 [z]: **CARDIOVASCULAR** *[Kreislauf Merkmale]*	**RRsys** [mmHG]	0.725	0.855		0.558	MED2 = -12.833 + RRdia * 0.075 + RRsys * 0.042 + RP * 0.022
	RRdia [mmHG]	0.740	0.824	**20.50**	0.480	
	RP [bpm]	0.162	0.395		0.255	R = 0.986
MED 3 [z]: **SUBJECTIVE** *[Beschwerden]*	**VAS** [cm; 0–10]	0.731	0.852		0.583	MED3 = 1.555 + VAS * 0.269 + EQ-VAS * -0.034
	EQ-VAS [%; 0–100]	0.732	-0.851	**17.09**	-0.581	R = 0.996
Unspecific Health Index *[Gesundheitszustandsindex]*	**UHI** [GZi]	**mean MED1, MED2 and MED3**			three factors	**70.83% VAR**

WC … waist circumference; RRsys/dia … blood pressure systolic/diastolic; RP … resting heart rate; VAS … Visuelle Analog Scale (Pain; 0–10); EQ-VAS… self-rated health (0–100); VAR … explained variance; High (positive) values [z] correspond to a worse expression.

Modified from (2, Tab.2) with permission of publisher © Georg Thieme Verlag KG

3.2.2 Health and Disease-Specific Indicators of an Inpatient Rehabilitation

The medical outcome factors presented in this thesis (see Table 2, p.15 and 2.2.1 Quantifying 'Medical Quality Outcome', p.25) represent valuable adjuncts to the assessment of the quality of medical outcomes. In addition to unspecific health factors (Table 3), disease-specific indicators were examined in more detail in the following manuscripts (3); the published work in Table 9 (3) placed a focus on multidisciplinary rehabilitation of the musculoskeletal system, while the submitted paper in Table 10 also included a consideration of various medical indications. The latter information has been presented in the form of posters or oral presentations at conferences (not quotable).

Table 9: Bibliographic information of paper '3' - Health and Disease-Specific Indicators.

Title What to Expect: Medical Quality Outcomes and Achievements of a Multidisciplinary Inpatient Musculoskeletal System Rehabilitation
Citation (3)* *(*. edited volume, open access peer-reviewed chapter – online first, October 17th 2019)* Grote, V., Unger, A., Puff, H., Böttcher, E. What to Expect: Medical Quality Outcomes and Achievements of a Multidisciplinary Inpatient Musculoskeletal System Rehabilitation. In: Bernardo-Filho M, Sá-Caputo D, Taiar R, editors. Physical Therapy Effectiveness [Working Title]: IntechOpen; 2019, online first. p. 27. doi:10.5772/intechopen.89596
Abstract The incidence of chronic diseases is rising. Rehabilitation plays a vital role in preventing and minimizing the functional limitations associated with chronic conditions and aging. Routine outcome measures include disease-specific and unspecific general health parameters. This study evaluates indicators for medical quality outcomes from 10,373 patients (61.00 ± 13.65 years, 51.7% women) which have undergone orthopedic rehabilitation for three weeks. Inpatient rehabilitation reduces life-style related risk factors, optimizes organ functioning and improves the well-being in the majority of patients (81.3%; SMD=0.52 ± 0.38). Improvements of unspecific and indication specific outcome parameters can be observed in a comparable magnitude. However, disease specific and unspecific health factors are not directly related to each other (r = .19). Age, gender, ICD-classification and time of rehabilitation have an influence on initial values and on indication-specific medical outcomes but are insignificant with regards to improvements in unspecific medical outcome parameters. Inpatient rehabilitation includes two main pathways of medical practice, which can be clearly distinguished in terms of their therapeutic outcome. There are general health interventions, such as lifestyle modifications, diet and physical exercise, and symptom-specific treatments. So multidisciplinary medical rehabilitation improves general well-being and physical functioning as well as reduces risk factors in the majority of patients.
Keywords Inpatient rehabilitation, medical quality outcomes, routine outcome measurement, reference data, rehab success;
Contribution to the dissertation and hypotheses Pronounced effects of inpatient rehabilitation can be observed for indication-specific characteristics. Improvements are achieved in the vast majority (81.3% of orthopedic patients for $MQO_{idx;}$ SMD = 0.52 +/- 0.38). Unlike unspecific health scores (UHI), moderating factors play a more important role in the specific outcome quality (ISI). In particular, patients who enter Phase II earlier (< 6 weeks) after surgery and patients with worse initial medical evaluation show better rehabilitation success in symptom-specific characteristics. We show that improvements in unspecific and indication-specific outcome indicators are of comparable magnitude and unspecific vs. disease-specific outcomes are not directly (linearly) related to each other (cf. 1.3.1 Derived Questions, p.19).
Special features, notes This work on orthopedic patients shows that inpatient rehabilitation comprises two main paths of medical practice that can be clearly distinguished with regard to their therapeutic result.

In addition to the usual "primary patient-oriented" assessment of quality of outcomes, we described two independent (active) components of rehabilitation. Unspecific health factors were expanded to disease-specific indicators, leading to a multidimensional view of specific and unspecific medical outcome quality (Figure 4). We assumed that the presented initial values and changes were representative of the inpatient rehabilitation of the musculoskeletal system in Austria.

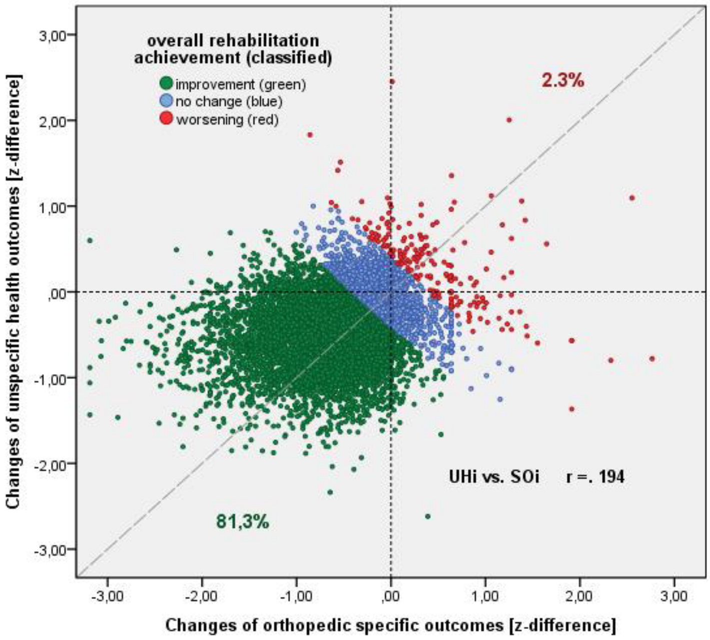

Figure 4: Correlative connection between unspecific and specific outcomes.

A value of zero (± 0.20 [z]) stands for no significant changes from admission to discharge (blue dots). The mean for UHI is -0.45 ± 0.43 and for ISI (SOi) -0.59 ± 0.55. The overall MQO_{idx} (mean of UHi & SOi) is -0.52 ± 0.38 (centroid).

Reproduced from (3, Fig.1)

Dependent on grouping characteristics (between-factors), this work showed that sex ($\eta^2_{multivariat}$ = .076), age ($\eta^2_{multivariat}$ = .067) and ICD classification ($\eta^2_{multivariat}$ = .080) contributed a significant amount to the initial medical values. Changes in the patient's condition from the pre- to the post-period could be observed within all grouping characteristics. Patients with knee and hip issues, patients who entered phase II earlier after undergoing surgery (< 6 weeks) and particularly older patients with worse initial medical values showed a more advantageous rehabilitation outcome for symptom-specific indicators. These results from orthopedic rehabilitation were confirmed using a larger and more heterogeneous data set (Table 4) for several different indications (Table 10 f.).

Table 10: Bibliographic information of paper 'a' - Health and Disease-Specific Indicators

Title Health and Disease-Specific Indicators React Differently to Inpatient Medical Rehabilitation - A Non-Randomized Controlled Routine Outcome Study in a Sample of over 16,000 Patients
Citation a* *(*. submitted manuscript)* Grote, V., Unger, A., Böttcher, E., Muntean, M., Puff, H., Marktl, W., Mur, E., Kullich, W., Holasek, S., Hofmann, P., Lackner, H.K., Goswami, N., Moser, M. Health and Disease-Specific Indicators React Differently to Inpatient Medical Rehabilitation - A Non-Randomized Controlled Routine Outcome Study in a Sample of over 16,000 Patients. Submitted 26/12/2019.
Abstract **Introduction:** Chronic diseases are increasing in modern society as the population ages. Rehabilitation plays a vital role in the prevention and minimization of the functional limitations associated with ageing and chronic conditions. **Methods:** The documentation process for patients who can benefit from rehabilitation needs to include the standardized collection of data based on performance indicators for medical quality outcomes. We summarized individual routine outcome measures to disease-specific or unspecific health indicators in a pre-post design that can be aggregated to obtain a total value for the medical quality outcome. Such data were collected from 16,966 patients (61.5 ± 12.5 years, 46.4% women) with different medical diagnoses in a non-randomized controlled trial. **Results:** Inpatient rehabilitation was shown to reduce the risk factors associated with certain lifestyles, optimize organ function and improve well-being in 77.9% of patients. The initial medical values obtained at the beginning of rehabilitation were influenced by indication, age and sex. However, these indicators are less significant with regard to improving unspecific health indicators. According to the disease-specific results, the greatest improvements were found in older patients (> 60 years) and during the early rehabilitation stage. **Conclusions:** To sustainably develop health services, clinical data and follow-up tests are needed to assess the success of therapies. Inpatient medical rehabilitation improves health for various indications to a comparable extent. Improvements occurred in two independent areas: general health determinants (risk factors) and disease-specific indicators for all indications and age groups.
Keywords Inpatient rehabilitation, medical quality outcomes, routine outcome measurement, age-related chronic diseases, influencing factors
Contribution to the dissertation and hypotheses Results of multiple individual medical outcomes from larger samples of patient data for different diagnoses are unavailable. We define two general medical success indicators for multidisciplinary rehabilitation that can be obtained from routine documentation: an unspecific and a disease-specific indicator. These main components develop differently after the primary medical intervention, but show similar improvements due to rehabilitation across different indications. Rehabilitation contributes to the greatest positive changes in older patients (> 60 years) and during the early rehabilitation stage. Inpatient rehabilitation works for nearly everybody (cf. 1.3.1 Derived Questions, p.19).
Special features, notes This manuscript summarizes potentially universal findings at the clinical trial center, which were presented in posters and oral presentations on conferences (not quotable).

This submitted paper shows for the first time that specific and unspecific health indicators behave differently during the time-delay between surgery and inpatient medical rehabilitation. Whereas specific health indicators improve, unspecific health indicators deteriorate over time if they are not treated in a rehabilitation program. The following section (p.34 to p.41) corresponds to the result section of the submitted work.

The effect of the rehabilitation stay (i.e., the change between the initial state and the discharge state) differed in terms of the individual success factors (UHI and ISI) for medical rehabilitation (Table 11). An examination of specific and unspecific outcomes shows a comparable change sensitivity (main effect time: $\eta_p^2{}_{\text{unspecific}}$ = .497 (UHI) vs. $\eta_p^2{}_{\text{specific}}$ = .475 (ISI), Table 12). The relationship between specific and unspecific outcome characteristics (changes) is small (*r* < .200, Figure 5), which is reflected in the results of a multivariate analysis of temporal changes in the variance ($\eta_p^2{}_{\text{multivariate}}$ = .624).

Table 11: Summarized medical quality outcomes and indication.

Unspecific Health Index (UHI) and Specific Index (ISI) formed the overall "Medical Quality Outcome" (MQO_{idx}) in equal parts. Aggregated medical outcome factors (UHI and ISI) showed a clear success during the rehabilitation stay in 77.9% of patients. Improvements in unspecific health factors (MED1, MED2, MED3) showed differences between indications, esp. for anatomy indicators (MED1), and discomfort (MED3). Changes in the averaged unspecific and specific indices are of comparable magnitude. Disease-specific parameters (ISI) could not be effectively compared between indications, because different medical parameters were used.

MQO: Medical Quality Outcomes - Rehabilitation WHO Phase II

[relative frequency in %]	indication	*initial state**	better	equal	worse	Ø-improvement**
overall **MQO$_{idx}$** UHI & ISI	Orthopedic	-1.6	81.3	16.4	2.3	*15.66 ± 11.36*
	Cardiovascular	4.0	71.2	26.1	2.7	*11.52 ± 9.75*
	Metabolic	-7.2	79.3	19.2	1.5	*12.55 ± 9.83*
	Oncology	9.7	78.6	19.3	2.1	*13.84 ± 10.46*
	Pulmonary	-0.3	74.6	22.0	3.5	*12.10 ± 10.01*
Medical Quality Outcome (MQO$_{idx}$)		**1.0**	**77.9**	**19.6**	**2.5**	***MQO$_{Index}$: 14.01 ± 10.85***
Threshold for classification: MQO$_{idx}$: ~ 0.33 (SMD)						
disease-specific	Orthopedic	0.9	77.0	19.0	4.0	*17.74 ± 16.00*
	Cardiovascular	4.2	56.6	39.8	3.6	*10.20 ± 12.48*
	Metabolic	7.0	64.8	31.3	3.9	*10.02 ± 11.29*
	Oncology	3.3	70.5	22.4	7.1	*13.67 ±14.82*
	Pulmonary	2.5	70.0	22.6	7.4	*12.64 ± 13.98*
Indication Specific Index (ISI)		**1.9**	**70.5**	**24.8**	**4.7**	***ISI: 14.70 ± 15.10***
unspecific	Orthopedic	-2.0	72.5	21.7	5.8	*13.58 ± 13.07*
	Cardiovascular	2.8	68.8	22.6	8.6	*12.83 ± 13.72*
	Metabolic	-15.0	75.7	16.6	7.7	*15.09 ± 15.06*
	Oncology	13.8	73.5	20.5	6.0	*14.01 ± 12.88*
	Pulmonary	-2.1	67.8	24.0	8.2	*11.74 ± 12.85*
Unspecific Health Index (UHI)		**0.5**	**71.4**	**21.8**	**6.8**	***UHI: 13.33 ± 13.27***
Threshold for classification: MED1–3: 0.20 (z-diff.), UHI: ~ 0.33 (SMD)						
[%]	**indication**	***initial state****	**better**	**equal**	**worse**	**Ø-improvement****
MED1	*Orthopedic*	1.2	11.3	86.4	2.3	1.34 ± 4.86
	Cardiovascular	-0.8	24.8	69.7	5.5	2.64 ± 6.52
	Metabolic	-23.5	47.4	51.5	1.1	3.45 ± 4.55
	Oncology	14.0	4.0	94.3	1.7	0.22 ± 3.92
	Pulmonary	1.3	5.1	93.1	1.8	0.41 ± 4.15
Shape (BMI, WC)		1.4	**14.1**	**83.1**	**2.8**	**MED1: 1.46 ± 5.15**
MED2	*Orthopedic*	1.1	56.5	15.7	27.8	11.47 ± 30.64
	Cardiovascular	2.0	60.6	11.3	28.1	15.76 ± 35.89
	Metabolic	-9.7	61.1	11.3	27.6	17.40 ± 35.15
	Oncology	9.5	60.3	12.6	27.1	13.86 ± 31.46
	Pulmonary	11.6	62.6	13.4	24.0	15.76 ± 32.05
Cardiovascular (RR, RP)		0.5	**58.7**	**13.9**	**27.4**	**MED2: 13.43 ± 32.35**
MED3	*Orthopedic*	-5.6	85.0	9.9	5.1	27.94 ± 23.33
	Cardiovascular	5.2	77.2	20.5	2.4	20.10 ± 19.55
	Metabolic	9.0	80.7	12.2	7.1	24.42 ± 29.06
	Oncology	5.0	87.1	10.7	2.2	27.95 ± 21.92
	Pulmonary	11.8	79.1	16.8	4.1	19.05 ± 19.55
Subjective (VAS, EQ-VAS)		0.6	**82.7**	**13.1**	**4.1**	**MED3: 25.11 ± 22.59**

WC … waist circumference; RR … blood pressure sys./dia.; RP … resting heart rate; VAS … Visuelle Analog Scale; EQ-VAS… self-rated health.

**. Initial state at the beginning of rehabilitation for monocentric normative data from the study center: A negativ percentile corresponds to a below-average (worse) value in the sample (n = 16966).*

***. Average improvement (percentile) from admission to discharge. 2016–2018 (N = 16.966): 61.52 ± 12.51 years Ø-age I 46.4% female / 53.6% male.*

The unspecific score – the "Health Index" (UHI; cf. Table 2 and Table 3) – shows that 71.4% of patients benefited directly from the rehabilitation stay, while 21.8% of the patients showed no improvement and the status of 6.8% worsened from the beginning to the end of the rehabilitation period (Table 11). A detailed analysis of improvement in UHI by 13.3 percentile points shows that shape features, such as the body mass index and waist circumference, remained unchanged over the three-week period for most of the patients (83.1%). In contrast, cardiovascular features, such as blood pressure and resting heart rate, seemed to be directly influenced by inpatient rehabilitation, with an average improvement of 13.4 percentile points observed. The most pronounced effects of inpatient rehabilitation could be seen by measuring the subjective features, whereby almost every indication (82.7%) reported a significant improvement. A similarly positive change is revealed by the indication specific score (ISI: +14.70 percentile points), whereby 70.5% of patients improved markedly.

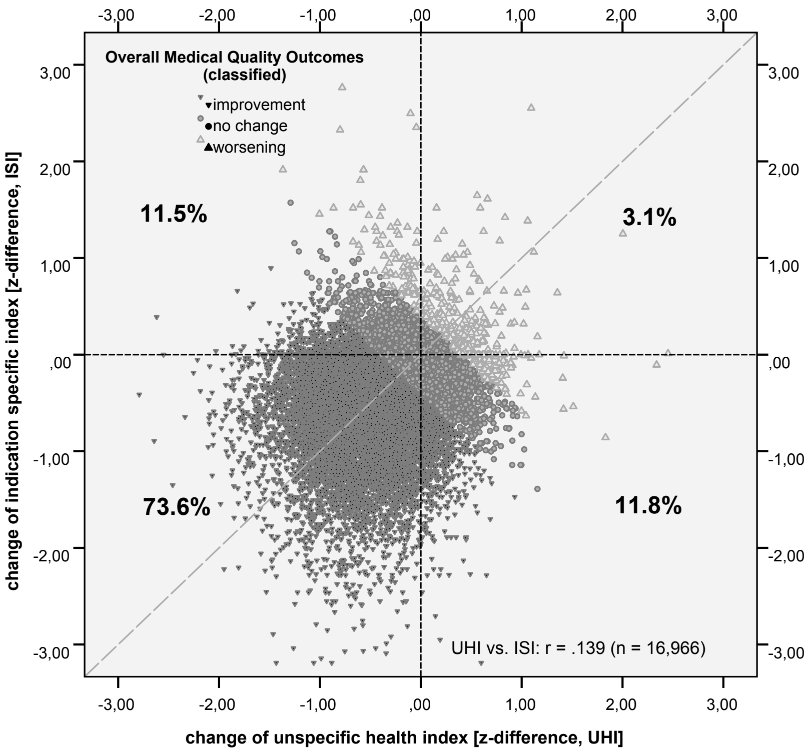

Figure 5: Improvements in unspecific and indication-specific medical outcomes.

The plot shows a marked improvement due to rehabilitation in specific as well as unspecific health indicators (cf. Figure 4). A value of zero ± 0.20 (z-difference) represents no significant changes from admission to discharge. Negative z-differences correspond to an improvement of the indicators. The mean for UHI is −0.45 ± 0.46 and for ISI −0.50 ± 0.53. The overall MQO_{idx} *(mean of UHI & ISI) is −0.48 ± 0.37 (centroid);* MQO_{idx}*:* d_{Cohen} *= -1.216,* $r_{pre\text{-}post}$ *= .77, CI 95% [-1.24, -1.19].*

Almost all considered medical factors (MED2, MED3, UHI, ISI) provide a comparable contribution to the overall success ($r \geq .50$; the only exception is MED1 vs. MQO_{idx}: $r = .123$).

The correlation between the unspecific index and specific index is low (r = .139; Figure 5). Therefore, immediate changes in unspecific health scores cannot be directly associated with improvements in (indication-)specific functional characteristics. One exception is the subjective complaints (MED3), which are related to specific outcome changes (r = .297). However, the extent of improvement in medical outcome and the effect size are similar in all areas (see Table 11, Table 12 and Figure 5). The shape factor (MED1) was the only factor that changed to a lesser extent during rehabilitation ($\eta_p^2{}_{MED1}$ = .080), due its smaller sensitivity to change (intra-individual variation) compared to inter-individual standard deviation.

Initial Values, Indication and Outcome

The assessed initial values (IV, baseline, pre) associated with rehabilitation clearly show the medical deficits of the affected patients. The average BMI is 28.7 ± 5.7 kg/m^2 (35.1% of patients had a BMI > 30 kg/m^2) and 77.4% of patients had a "high-normal" (22.2%) or "hypertonic" (52.2%) blood pressure (mean $RR_{sys/dia}$: 131.1/77.3 ± 14.3/8.4 mmHG). The perceived pain (VAS; 0–10) of the patients was 2.8 ± 2.4, and the subjective health status (EQ-VAS; 0–100) was estimated as 62.1 ± 17.0% on average.

Unspecific and indication-specific outcome data (Table 11, Table 12) show clear successes as a result of inpatient rehabilitation, with overall medical quality outcomes [MQO_{idx}: η_p^2 = .622 (e.g., subjective self-evaluation (MED3: η_p^2 = .564)] improving markedly within the three- to four-week period. Indication played a role in these improvements, especially with regard to the shape indicators (MED1: η_p^2 = .046), subjective complaints (MED3: η_p^2 = .030) and indication specific indicators, although the latter could not be effectively used to compare between indications because different medical parameters were used. Improvements in the Unspecific Health Index (UHI: η_p^2 = .004) showed only a slight dependency on indication. If one considers the changes that occurred between admission and discharge as a result of the inpatient rehabilitation stay, the baseline values ("IV"), indication ("IND") and admission diagnosis ("ICD", Table 12 and Table 5) also need to be evaluated.

Table 12: Effect sizes for MQO and moderating factors.

Sex, indication and diagnoses played roles in initial values of body shape (MED1; η_p^2 > .07). In particular, the patient age influenced the disease-specific baseline values (ISI; η_p^2 = .079), but did not play a major role in terms of rehabilitation success (changes; all η_p^2 < .01). An examination of specific and unspecific outcomes revealed a comparable change sensitivity (main effect time: $\eta_p^2{}_{UHI}$ = .497 vs. $\eta_p^2{}_{ISI}$ = .475. Changes in unspecific health index showed only a slight dependency on indication ($\eta_p^2{}_{UHI}$ = .004), which is more important for disease-specific improvements ($\eta_p^2{}_{ISI}$ = .035).

η_p^2	unifactorial part. Eta² for **initial values** (pre)*						unifactorial part. Eta² for **changes** (post-pre; interaction)**								main effect
between-factors	**sex**	**age**	**IND**	**no. diag.**	**dropout**	**ICD**	**sex**	**age**	age	**IND**	**no. diag.**	**ICD**	ICD	**IV_{MQO}**	**time**
MQO variables	f/m	5-stage	5-stage	3-stage	2-stage	32-stage	f/m	5-stage	cov. IV	5-stage	3-stage	32-stage	cov. IV	3-stage	2-stage
MED 1: Shape	.032	.012	.077	.007	.000	.141	.008	.002	.004	.046	.002	.055	.054	.008	.079
MED 2: Cardiovascular	.014	.009	.045	.004	.000	.062	.002	.003	.004	.010	.002	.016	.021	.027	.149
MED 3: Subjective	.018	.012	.044	.002	.002	.070	.009	.001	.001	.030	.000	.040	.042	.044	.564
Unspecif. Health (UHI)	.010	.016	.055	.010	.001	.087	.000	.002	.005	.004	.001	.011	.017	.069	.497
Indication Specific (ISI)	.026	.079	.006	.018	.007	.063	.007	.009	.002	.035	.023	.069	.062	.109	.475
Overall MQO_{idx}	.003	.055	.021	.022	.006	.054	.003	.005	.001	.016	.009	.030	.028	.156	.622

Between factors: sex (female, male), age (<= 40, 41–50, 51–60, 61–70, 71+), IND … indication (ORT, CAR, PUL, MET, ONC), no.diag. … number of diagnoses (1, 2, > 2), dropout (regular vs. < 18 days), ICD … 32 main-diagnoses (see Tab. 5), IV … initial value MQO (tertile); cov. ... covariate; a part. Eta² (η_p^2) between .01–.06 corresponds to a small effect, occurrences of .06–.14 a middle effect and values > .14 a large effect.

**. Initial state (pre) at the beginning of rehabilitation;*
***. Differences (improvements; post-pre) from admission to discharge (corresponds to the interaction: time x factor);*

A closer look on individual diagnoses show that metabolic patients (E11, E66, E14) have worse initial shape values (percentile $MED1_{\text{initial state (IV)}}$ = -23.5, Table 11; η^2_{ICD} = .141, Table 12) but also the strongest improvements for this factor ($MED1_{PUL}$: 47.4% of patients show improvement, Table 11; interaction: η^2_{ICD} = .055, Table 12). Cardiac patients, especially those with essential (primary) hypertension (I10), pulmonary patients (J44, J45, I26 J84) and again metabolic patients (E66, E14) had more critical cardiovascular initial values ($MED2_{IV}$: z > .60 vs. overall $MED2_{IV}$: z = 0.20 ± 1.06), with the most pronounced improvements seen for patients with I10 ($z_{diff.}$ = -1.16) and E66 diagnoses ($z_{diff.}$ = -0.82) and the smallest effects seen for patients with type 1 diabetes (E10: $z_{diff.}$ = -0.19; overall $z_{diff.}$ for MED2: -0.49 ± 1.15). Orthopedic patients with dorsalgia (M54) and patients with S72, M19 and M48 reported severe subjective complaints at baseline ($MED3_{IV}$: z >.55 vs. overall $MED3_{IV}$: z = 0.24 ± 0.93), which were also high for patients with malignant neoplasm of the bladder (C67: z = 0.59) and lowest for patients with asthma (J45: z = -0.24). Cardiac and pulmonary patients showed weaker improvements in their complaints (MED3: $z_{diff.}$ ~ -0.60) than orthopedic or cancer patients ($z_{diff.}$ ~ -0.90).

Overall, improvements are clearly visible for all factors, indications and diagnoses (Table 11 and Table 12). These findings indicate that rehabilitation is generally successful (time: η^2_{UHI} = .497) if a comparable scale is used between diagnoses (time x ICD: η^2_{UHI} = .011, with initial values of MQO_{idx} as a covariate: η^2_{UHI} = .017), although the changes observed depended on the initial values used (time x IV_{MQO}: η^2_{UHI} = .069; UHI: $r_{\text{pre vs. post-pre}}$ = -.492), which differed significantly between the diagnoses for unspecific baseline values (ICD_{IV}: η^2_{UHI} = .087).

Age as an Influencing Factor

Upon the examination of further grouping characteristics (between-factors), we observed that sex ($\eta^2_{multivariat}$ = .071) and age ($\eta^2_{multivariat}$ = .026) contributed significantly to the initial values, which are lower within unspecific than within specific parameters. In contrast, age and sex played minor roles in influencing medical outcome indicators (age: η^2_{MQO} = .003, sex: η^2_{MQO} = .005, Table 12).

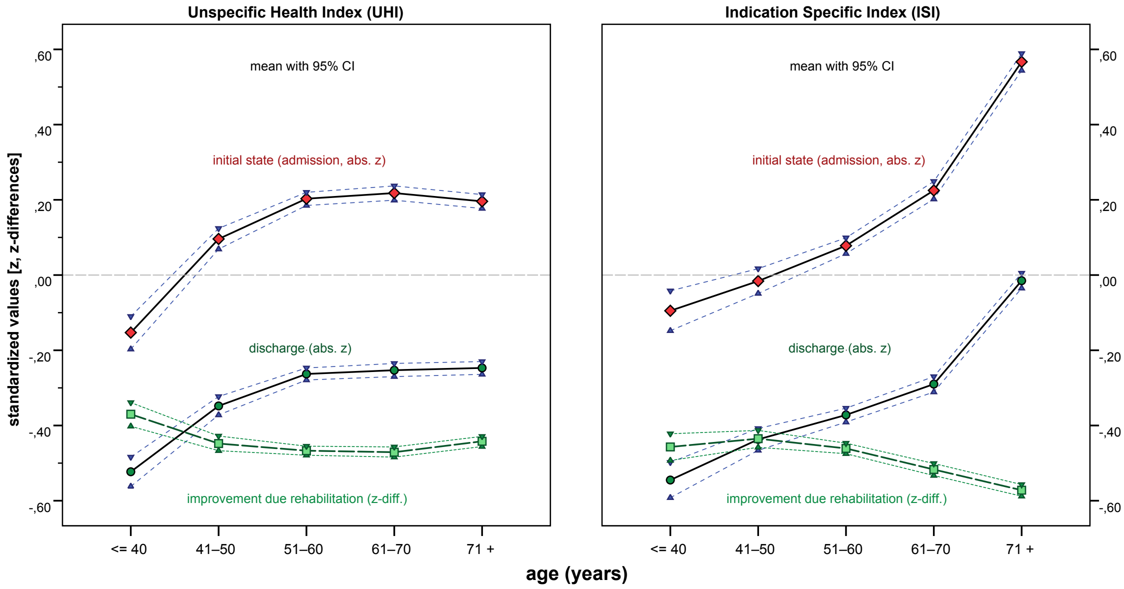

Figure 6: Changes due to rehabilitation depending on the subjects' ages.

Age contributed significantly to the initial values, which were lower within unspecific than within specific parameters. Improvements in older subjects were equal or even stronger, especially in terms of specific health indicators. Changes due to inpatient rehabilitation were strong for all age groups.

Older patients (> 60 years) showed an equal or even more favorable symptom-specific outcome (*z*-difference $_{ISI}$: 0.55 ± 0.55 vs. 0.50 ± 0.53; Figure 6). Younger patients (< 51 years) showed better baseline values for all medical parameters (Table 13 and Figure 6), which is associated with a lower potential for change. Nevertheless, the equal or even more marked improvements seen in older patients (> 60 years; *z*-difference $_{MQO}$: 0.50 ± 0.38 vs. 0.48 ± 0.37) persisted, even when the initial states were taken into account (Table 12). The effects of age on rehabilitative outcome was not the same in all indications. Especially older orthopedic patients were shown to gain the strongest benefit in overall MQO_{idx}, whereas younger cardiovascular patients showed the lowest response to rehabilitation therapy (see Figure 6 and Figure 7).

Table 13: Summarized medical quality outcomes and age.

Age contributed a significant amount to initial states but played a minor role in altering medical outcome indicators. Older patients (> 60 years) showed equal or even more favorable symptom-specific outcomes. Younger patients (< 51 years) showed better baseline values for all medical indicators.

MQO: Medical Quality Outcomes and Age

[relative frequency in %] *Threshold for classification ~ 0.33 SMD*	*age*	*initial state**	**better**	**equal**	**worse**	Ø-improvement**
overall UHI and ISI	**<= 40**	16.7	74.3	22.0	3.6	*12.45 +/- 10.93*
	41–50	8.8	75.4	22.0	2.6	*12.88 +/- 10.51*
	51–60	3.9	77.9	19.5	2.6	*13.72 +/- 10.57*
	61–70	-0.1	78.6	19.3	2.0	*14.52 +/- 10.91*
	71+	7.9	79.2	18.4	2.4	*14.70 +/- 11.18*
Medical Quality Outcome (MQO_{idx})		**1.0**	**77.9**	**19.6**	**2.5**	***MQO*** $_{Index}$ ***: 14.01 +/- 10.85***
disease-specific	**<= 40**	13.8	67.8	26.3	5.9	*13.85 +/- 15.19*
	41–50	10.7	65.6	28.6	5.8	*12.95 +/- 14.91*
	51–60	7.1	69.3	25.5	5.2	*13.85 +/- 14.52*
	61–70	1.8	71.5	24.8	3.7	*15.34 +/- 15.03*
	71+	-10.2	73.6	22.0	4.4	*16.05 +/- 15.73*
Indication Specific Index (ISI)		**1.9**	**70.5**	**24.8**	**4.7**	***S*** $_{Index}$ ***: 14.70 +/- 15.10***
unspecific	**<= 40**	14.5	67.6	23.5	8.9	*11.06 +/- 12.58*
	41–50	3.9	71.4	22.1	6.5	*12.81 +/- 12.83*
	51–60	-0.7	72.6	20.9	6.5	*13.59 +/- 13.21*
	61–70	-1.4	72.1	21.4	6.5	*13.70 +/- 13.35*
	71+	-0.6	70.1	22.9	7.0	*13.35 +/- 13.55*
Unspecific Health Index (UHI_{MED1-3})		**0.5**	**71.4**	**21.8**	**6.8**	***UH*** $_{Index}$ ***: 13.33 +/- 13.27***

2016–2018 (N=16966): 61.52 +/- 12.51 years Ø-age I 46.4% female / 53.6% male

**. Initial state at the beginning of rehabilitation: A negativ percentile corresponds to a below-average (worse) value in the total sample.*

***. Average improvement (percentile) from admission to discharge.*

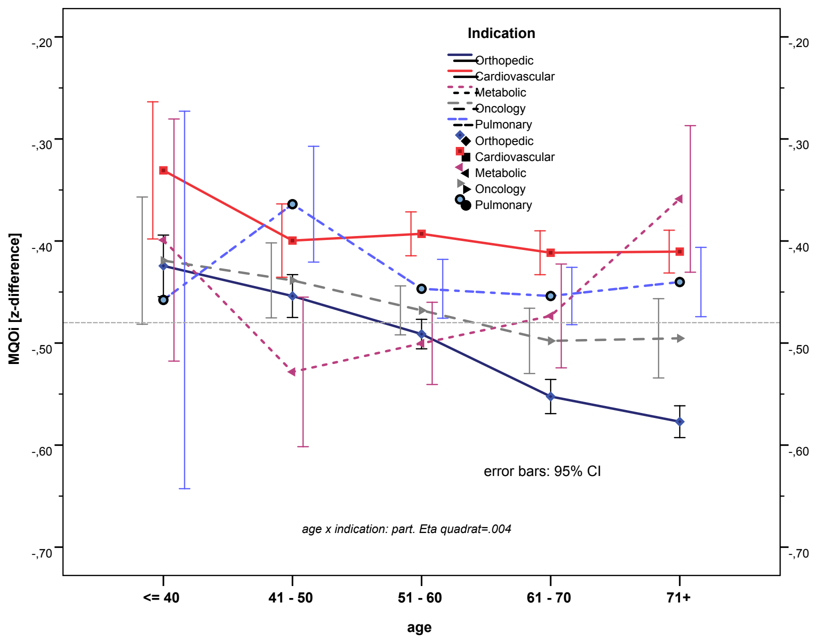

Figure 7: Medical quality outcome depending on indication (color) and age (abscissa).

All rehabilitation types were medically successful and improved the patients' conditions by an average of −0.48 ± 0.37 (MQO_{idx}). The strongest increase in improvement with age was observed for the orthopedic, followed by cardiovascular and oncologic, rehabilitation patients. Metabolic rehabilitation showed best results for patients aged 41–50. Pulmonary and metabolic rehabilitation did not show clear associations with age.

Timing of Rehabilitation

In the subsample of orthopedic patients who had undergone knee, hip, or shoulder surgery and cardiovascular patients with chronic ischemic heart disease and non-rheumatic aortic valve disorders (see Table 6), we observed that changes occurred in the UHI, independent of the time delay until rehabilitation was initiated (interaction: time x post-op week: η_p^2 = .003).

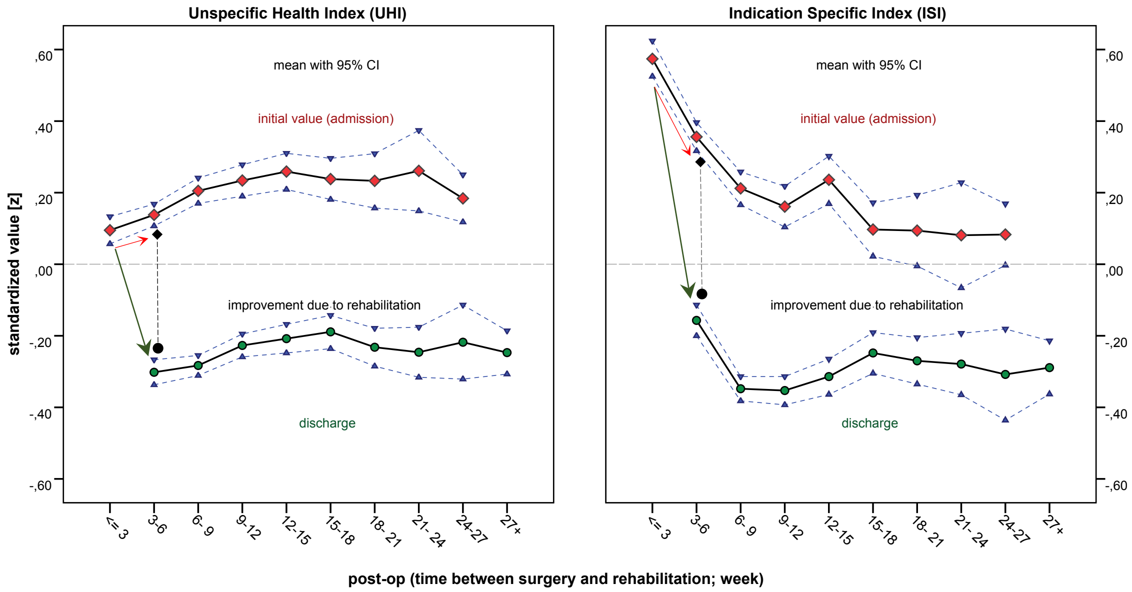

Figure 8: Influences of time delay between surgery and rehabilitation.

Whereas unspecific health indicators (left) became worse (going up) as the time delay until surgery increased, specific (right) indicators improved (going down) by natural self-reorganization of the body. The odds ratio (OR) for spontaneous improvements without rehabilitation (red) is 0.74 for UHI and 3.20 for ISI. All indicators improved markedly stronger by rehabilitation (green arrows) than by the time delay (red arrows and abscissa). The rehabilitative success (distance between upper and lower lines) of unspecific health indicators (left) was not strongly influenced by the time delay between surgery and rehabilitation, whereas the improvement due to rehabilitation of specific health indicators (right) decreased with the increasing delay, indicating that an early onset of medical rehabilitation is beneficial. Data for this figure were obtained from a subsample of orthopedic and cardiovascular patients that had undergone surgery (n = 5453) and had been given the following diagnoses: M16, M17, M75 and I25, I35 (see Table 6).

Patients who began rehabilitation later had initially better specific indicators in contrast to unspecific health indicators (initial value: $\eta_p^2{}_{ISI}$ = .042 vs. $\eta_p^2{}_{UHI}$ = .009; Figure 8 and Table 14). However, the later these patients entered phase II rehabilitation, the lower their observational specific success was ($\eta_p^2{}_{ISI}$ = .062). These results applied equally to orthopedic and cardiovascular patients (interaction: indication x post-op week: $\eta_p^2 < .009$), independent of their age, initial state, or diagnoses, but were more pronounced in orthopedic patients (time x indication: $\eta_p^2{}_{ISI}$ = .047).

Table 14: Effects of timing on a phase II rehabilitation.

Changes occurred in the unspecific factor independent of the time of rehabilitation ($\eta_p{}^2{}_{UHI}$ = .003), in contrast to disease-specific outcome characteristics (ISI), whereby the time of onset (post-op week) played a more important role ($\eta_p{}^2$ = .062). These results apply equally to orthopedic and cardiovascular patients (interaction: indication x post-op week: $\eta_p{}^2$ < .009), but were more pronounced in orthopedic patients (time x indication: $\eta_p{}^2{}_{ISI}$ = .047).

part. Eta ^{2} ($\eta_p{}^2$) n = 5453 (M16, M17, M75 & I25, I35)		initial value* postOP (9-stage)	changes (post-pre)** time	time x post-op	indication (2-stage)	indication x postOP
Unspecific Health	(UHI)	.009	.356	.003	.000	.002
Indication Specific	(ISI)	.042	.335	.062	.047	.008
overall Medical Quality Outcome	(MQO_{idx})	.011	.479	.024	.021	.007

Between factors: post-op (cf. Fig. 8) ... timing rehab.: < 3, 3–6, 9–12, 12–15, 15–18, 21–24, 24+ weeks; indication: orthopedic vs. cardivascular.

*. Initial state (pre) at the beginning of rehabilitation;

**. Differences (improvements; post-pre) from admission to discharge;

3.3 Cardiac Autonomic Control and Dynamic Temporal Changes

For ethical, practical and economic reasons, rehabilitation studies can not only address individual forms of therapeutic applications or work with "real" control groups, as would be desirable from a scientific point of view. Evidence-based medical research and demands for proof of effectiveness and the sustainability of individual treatments in inpatient rehabilitation are, therefore, often the result of a compromise, because one cannot simply withhold established and proven medical offerings from a patient.

In addition to standard methods and established medical indicators, heart rate variability is a promising physiological variable that can be used for the evaluation of medical treatments and dynamic temporal changes over time, as well as for the sustainability of rehabilitation programs. Measuring cardiac autonomic control can be reliably done by analyzing the heart rate variability (HRV). HRV is created by the interaction between autonomic nervous system (ANS) and the sinus node of the heart (154-157). A more detailed description of HRV methods and parameters can be found in V. Grote, 2009 (158, pages 65 to 70).

3.3.1 Single Therapy Applications

Table 15: Bibliographic information of paper '1' - Single Therapy Applications.

Title Vibration Therapy in Orthopaedic Rehabilitation - Evaluation of in-Patient Rehabilitation Measures in Orthopaedic Patients Using a Mechanical Vibration Couch
Citation (1) Grote, V., Böttcher, E., Zahirovic, S., Moser, M., Puff, H. (2018). Vibration Therapy in Orthopaedic Rehabilitation - Evaluation of in-Patient Rehabilitation Measures in Orthopaedic Patients Using a Mechanical Vibration Couch. Phys Med Rehab Kuror, 28(03), 171-183. doi:10.1055/a-0584-0168
Abstract **Purpose.** Clinical uses of mechanical whole body vibration therapies are the subject of contradictory debate. Orthopaedic pathologies, including the presence of endoprostheses, are considered to be contraindications. **Materials and Methods.** Within the context of a 3-week inpatient rehabilitation programme 109 orthopaedic patients (61.4 ± 8 years) were stratified to one of the trial groups: vibration therapy couch (Tiktaalik), dry water massage (Hydrojet) and sham treatment (placebo). Effects on the quality of medical results and heart rate variability were examined. **Results.** The therapy had a duration of 12 minutes. The vibration frequency of the treatment couch was self-selectable between 11 and 15 Hz in the chest region and 3 and 7 Hz in the pelvic region. Two patients had to stop the vibration therapy early (headaches, dizziness). The rehabilitation measures allowed mobilisation, leading to increased activation of the sympathetic nervous system. Improvements in pain perception (VAS) and motor function (flexibility, muscle strength) were identified during the course of the rehabilitation. An interaction of the rehabilitation process with the trial groups was observed immediately after each unit of therapy: The flexibility, muscle strength and alertness improved more markedly in the Tiktaalik group. At the same time the mechanical vibration therapy distinguished itself particularly by more marked parasympathetic modulation - there was significantly greater relaxation in the post-treatment rest phase. **Discussion and Conclusions.** The study results show that mechanical vibration therapy represents an addition to the currently available treatment options for orthopaedic rehabilitation.
Keywords Orthopedics, rehabilitation, heart rate variability, vibration couch, whole body vibration (WBV);
Contribution to the dissertation We used heart rate variability for development and evaluation of a new medical treatment (mechanical vibration therapy). Mechanical vibrations can influence the metabolism and (muscle) activity of the human organism. We show that cardiac autonomic control is well suited to describe different therapeutic applications and effects within a rehabilitation setting even without a 'real' (untreated) control group. Evidence-based therapy applications and clinical trials are a prerequisite for a successful recovery process of a rehabilitation patient.
Special features, notes Randomized sample of orthopedic patients with additional measurements and treatments out of routine.

Over the course of the rehabilitation, a continuous increase in vegetative (autonomic) activity can be observed, which can be interpreted as a consequence of the physical mobilization (4, 159). Due to the numerous and proven therapeutic offers during rehabilitation, it is normally not possible to evaluate the potential effects of a single application on the basis of the changes from admission to discharge, as presented for the results of routine outcome measurements in this work. It is, therefore, necessary to take a closer look at the individual therapy units and the period immediately before and after the application (see Figure 9).

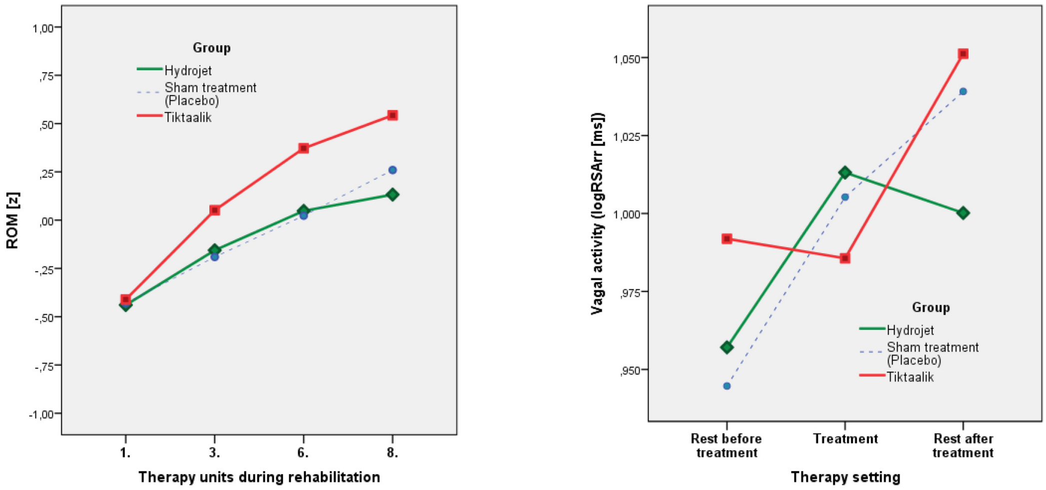

Figure 9: Range of Motion (ROM, left) and vagal activity (logRSArr, right) over time

In contrast to an overwater massage (Hydrojet), both the specificity of mechanical vibration therapy (Tiktaalik) and an immediate better effect on functional motor functions is noticeable through a stronger vagal modulation (logRSArr).

Modified from (1, Fig.4 & Fig.5) with permission of publisher © Georg Thieme Verlag KG

The principle of the provision of a series of regular therapeutic stimuli, like mechanical vibration therapy or an inpatient rehabilitation, in general lead to functional adaptations, which are characterized by improvements in regulatory qualities and the economization and normalization of physiological functions. The hypothesis that higher vagal activity, a more pronounced reaction, or a greater circadian dynamic (amplitudes, oscillations) are associated with better health or recovery was tested in the next article (Table 16).

3.3.2 Temporal Changes

Longitudinal Measurement of Circadian Vagal Tone

Table 16: Bibliographic information of paper '4' - Temporal Changes.

Title Dynamics of Vagal Activity Due to Surgery and Subsequent Rehabilitation
Citation (4) Grote, V., Levnajic, Z., Puff, H., Ohland, T., Goswami, N., Fruhwirth, M., Moser, M. (2019). Dynamics of Vagal Activity Due to Surgery and Subsequent Rehabilitation. Front Neurosci, 13(1116). doi:10.3389/fnins.2019.01116
Abstract **Background:** Vagal activity is critical for maintaining key body functions, including the stability of inflammatory control. Its weakening, such as in the aftermatch of a surgery, leaves the body vulnerable to diverse inflammatory conditions, including sepsis. **Methods:** Vagal activity can be measured by the cardiorespiratory interaction known as respiratory sinus arrythmia or high-frequency heart-rate variability (HRV). We examined the vagal dynamics before, during and after an orthopedic surgery. 39 patients had their HRV measured around the period of operation and during subsequent rehabilitation. Measurements were done during 24h circadian cycle on ten specific days. For each patient, the circadian vagal tone was calculated from HRV data. **Results:** Our results confirm the deteriorating effect of surgery on vagal tone. Patients with stronger pre-operative vagal tone suffer greater vagal withdrawal during the peri-operative phase, but benefit from stronger improvements during post-operative period, especially during the night. Rehabilitation seems not only to efficiently restore the vagal tone to pre-operative level, but in some cases to actually improve it. **Discussion:** Our findings indicate that orthopedic rehabilitation has the potential to strengthen the vagal activity and hence boost inflammatory control. We conclude that providing a patient with a vagal reinforcemnet procedure prior to the surgery ("pre-habilitation") might be a beneficial strategy against post-operative complications. The study also shows the clinical usefulness of quantifying the cardiorespiratory interactions.
Keywords Circadian rythm, surgery, vagal tone, inflammatory control, rehabilitation;
Contribution to the dissertation and hypotheses This study relies on a longitudinal measurement and comparison of circadian dynamics (24 h recordings) of cardiac autonomic control (HRV, vagal activity) in patients before, during and after a surgical procedure. This includes measurements during and after rehabilitation, for up to 1 year after the surgery. We show that regular vagal activity is not only restored but also enhanced by the process of the rehabilitation. In addition to rehabilitation, a "pre-habilitation" of patients scheduled for surgical treatments appears to be a good strategy for avoiding peri-operative complications like sepsis. We present dynamic temporal changes relating to an inpatient rehabilitation and show that vagal activity plays an important role.
Special features, notes Specific sample of orthopedic patients with additional measurements out of routine; we used circadian heart rate variability measurements for quantifying temporal cardiac autonomic changes during an operation-rehabilitation process.

In addition to the reported general positive routine outcome of rehabilitation, significant and sustainable improvements could be observed up to a year after the primary treatment (phase I). Standardized indicators for HRV, complaints and sleep recovery showed significant improvements (158-160), while a cardiac autonomic regulation comparable to that of healthy controls could only be achieved after one year (see Figure 10).

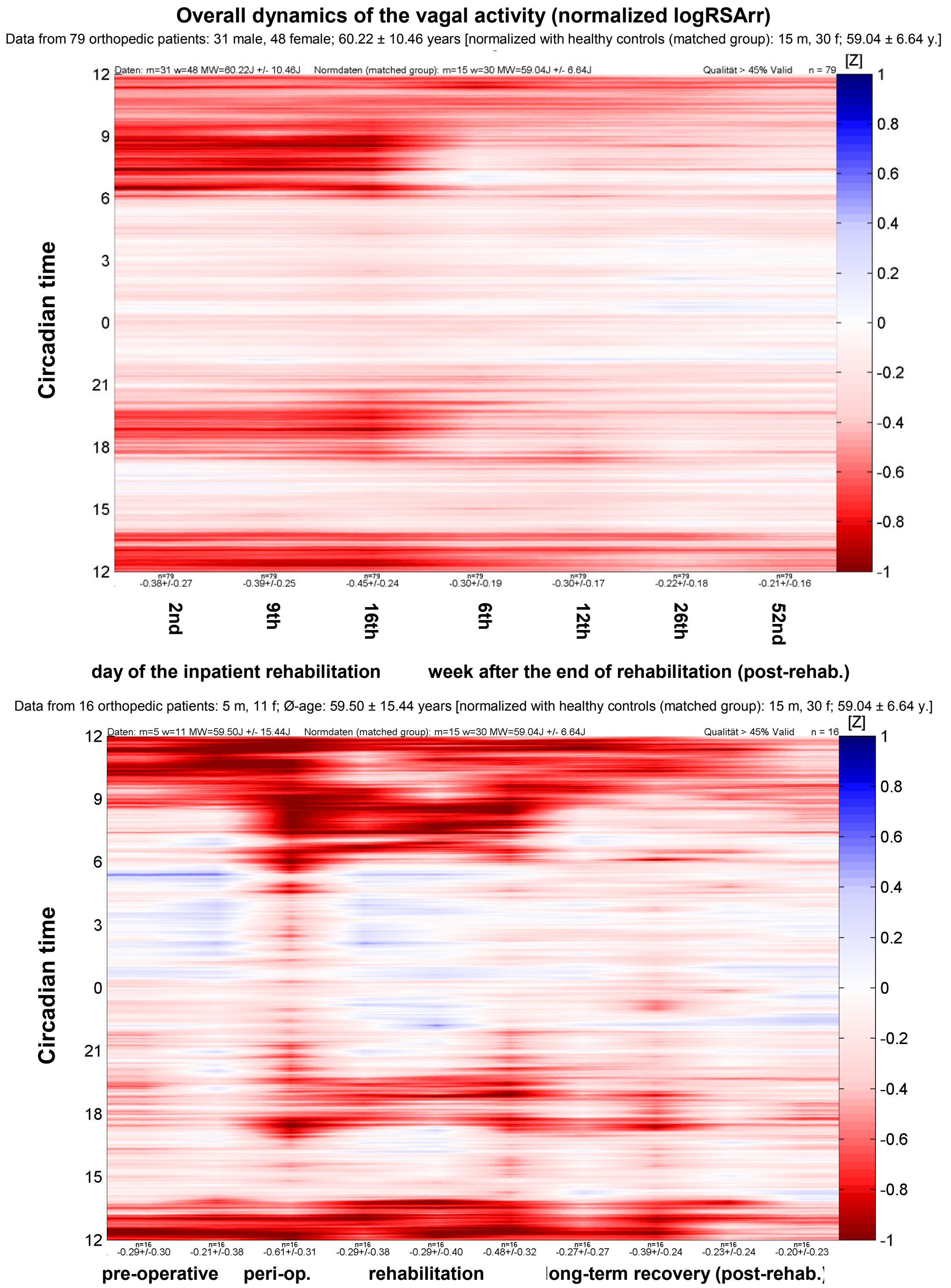

Figure 10: Longitudinal measurement of circadian rhythm of normalized vagal activity.

Each color represents the value of the vagal activity averaged over all available orthopedic patients on a given measurement day (horizontal axis) and at a given circadian hour (vertical axis, time runs from bottom to top). Each averaged vagal activity value is represented as a color, where red means low, blue means high vagal activity and white (Z = 0) corresponds to age and sex matched reference values from healthy controls (see color bar). After rehabilitation, vagal activity is gradually restored, similar to that of healthy individuals.

Reproduced from (159, Fig.4), modified from (4, Fig.2)

Outpatient Phase III Cardiac Rehabilitation

Further follow-up in cardiovascular rehabilitation takes place as an outpatient (phase III; Figure 1). Exercise training is carried out over a time period of six to twelve months in order to extend maximal physical capacity and to change the patient's lifestyle. In a conference contribution (5), we presented the medical outcomes of 140 cardiovascular phase III patients with a preceding inpatient phase II at the clinical trial center (cf. p.21).

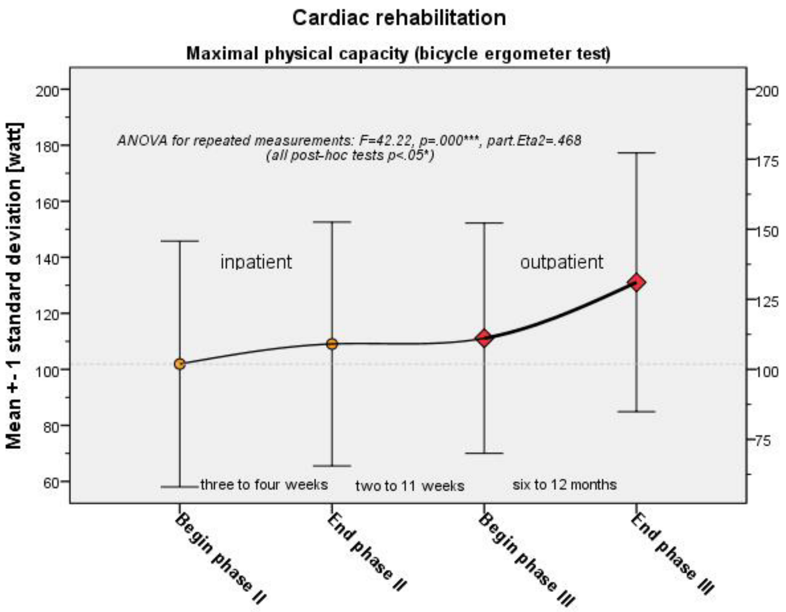

Figure 11: Further improvements in physical capacity in phase III patients.

The average age of the 140 patients with stable cardiovascular disease was 62.4 ± 10.3 years, with women accounting for 26.4% of subjects. The phase III patients attended a phase III follow-up session at 6.3 +/- 4.3 weeks on average after the inpatient phase II. This lasted for 29.3 ± 9.2 weeks, with a total of 48.1 ± 13.8 units of outpatient therapy carried out. Physical fitness improved by 19.1 ± 20.5 Watts (from 111.9 to 131.0 Watts) in phase III.

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By summarizing the compulsory clinical data as an overall medical quality outcome (MQO_{idx}; cf. 2.2.1 Quantifying 'Medical Quality Outcome', p.25), only 36% of patients improved during the phase III intervention, 56% of patients showed no changes, and 9% showed a worsening of their health by the end of phase III. It is only possible to say that the majority of the patients stabilized at a good level if the results of phase II are taken into account. Body weight was shown to increase in approx. 44.3% of patients over the course of phase III (average weight increase: 1.6 ± 3.3 kg). In addition to physical fitness (Figure 11), the quality of life improved considerably ($p < .001$). This was reflected in the high rates of patient satisfaction (95%) with the outpatient version.

3.4 Medical Quality Outcomes - Lifestyle and Physical Activity

3.4.1 GVA

The risk of developing chronic diseases can be minimized by up to 50% by practicing an active lifestyle (36). Almost all non-communicable diseases can be treated by therapies, including physical activity and strengthening programs (40). Exercise therapy, thus, has become the golden standard among medical treatments for a multitude of chronic diseases.

Table 17: Bibliographic information of paper 'b' - Lifestyle and Physical Activity.

Title An Inpatient Health Care Program for Musculoskeletal Disorders to Improve Well-being in Patients with Chronic Conditions
Citation b* *(*. submitted manuscript)* Grote, V., Unger, A., Hofmann, P., Marktl, W., Holasek, S., Moser, M., Böttcher, E. An Inpatient Health Care Program for Musculoskeletal Disorders to Improve Well-being in Patients with Chronic Conditions. Submitted 13/12/2019.
Abstract **Introduction:** In 2014, an inpatient secondary preventive program for patients with musculoskeletal health problems was introduced, which was expanded throughout Austria after April 2018. The aim of the current work was to evaluate this program [called "GVA," Gesundheitsvorsorge Aktiv (Health Care Active)] and its possible influences on the quality of medical results at hospital discharge. **Method:** In this paper, monocentric data are presented for patients who completed a three-week GVA program between January 2016 and January 2019, placing a focus on medical quality outcomes such as BMI, blood pressure, heart rate, pain, subjective ratings and achieved power output on the cycle ergometer. The mean age of 7,488 patients was 48.99 ± 6.15 years, and 53.7% of included subjects were women. The average duration of the inpatient health stay was 21.73 ± 1.85 days. **Results:** At the beginning of the program, the medical baseline showed obvious deficits regarding obesity, hypertension and subjective symptoms. Of all patients, 36.3% were completely inactive. Sex and physical activity had a high impact on the medical baseline status. In total, the majority of patients (86.3%) responded well to the health care program, independent of their ages and lifestyles. Men improved more than women with respect to parameters like blood pressure or physical capacity. **Discussion:** The results of the study reflect the general problems presented by inactivity, obesity and subjective symptoms like pain, as well as the need for gender-specific considerations. Physical activity was specifically identified as a major factor for the observed medical baseline status. Overall, risk factors could be reduced by the inpatient secondary preventive program. The patients' physical capacities and quality of life significantly improved. Requirements for secondary preventive programs such as the GVA are high. Future studies should be carried out to clarify whether further support for sustainability is needed.
Keywords Prevention, health care, medical quality outcome, routine outcome measurement, physical activity;
Contribution to the dissertation and hypotheses A new active health care program (GVA) with a medical-secondary preventive focus replaces the classical, three-week-long, medical spa therapy in Austria. The evaluation of the GVA program showed that patients had deficits in general risk factors, such as reduced physical activity, hypertension and obesity. Participation in the program resulted in similar improvements in almost all patients. We show that patient characteristics such as sex and pre-treatment physical activity have a significant impact on baseline medical status. The majority of patients benefit from an inpatient health care (cf. 1.3.1 Derived Questions, p.19). The results highlight the need for physical activity.
Special features, notes This manuscript summarizes findings of the new active health care program (GVA), which were presented in posters and oral presentations on conferences (161-164). Additionally we made a post survey in a random subsample one year after, with a response rate of 31.6%. With a return to everyday life, the successes of the secondary preventive program have declined significantly, but are still observable after one year.

In 2018, after being tested over a three-year pilot period, an active health care program (GVA) with a medical-secondary preventive focus replaced the classic, three-week medical spa therapy in Austria. The modular structure of the GVA places a demand-oriented focus on exercise (motivation and optimization) and mental health and is characterized by an increased proportion of active therapies. Active treatments consist of physical activity, including gymnastic and individual physiotherapy sessions; the training therapy emphasizes underwater, ergometer, Nordic-walking, strength, balance, relaxation and motion training. Each patient can take part in a program that includes a minimum of 1400 minutes therapy over a three-week period (Table 1).

Inpatient rehabilitation and GVA are different in that the GVA plays a more preventive role. Compared to patients who enter an orthopedic rehabilitation, GVA patients are generally younger and do not yet display disorders of the musculoskeletal system, which would require special rehabilitation treatments. The ICD classification of degenerative, inflammatory musculoskeletal complaints is similar in GVA and orthopedic patients, as is the chronic impairment of their functional capacity and health (2, 3). However, GVA patients have not experienced acute events, received care, or undergone recent surgical interventions (WHO Phase I) on the musculoskeletal system.

Physical Activity

In addition to the usual medical indicators (see Table 2), patient information on physical activity in everyday life was recorded. Male patients reported performing slightly more overall physical activity before they started their inpatient stay than women (3.03 ± 4.13 vs. 2.80 ± 3.58 hours per week; $\eta_p^2 = .001$, $p = .011$)[4]. Of all GVA patients ($n = 7{,}448$; Table 4), 36.3% were not physical active at all, and 20.0% exercised less than 120 minutes a week. Older patients (56+ years) were somewhat more physical active ($\eta_p^2 = .002$). Physical activity was lower in obese patients ($\eta_p^2 = .018$). The diagnosis themselves played minor roles according to physical activity ($\eta_p^2 = .003$) (e.g., patients with disc disorders (M51, M50) were less active). The strongest dependency with physical activity (PA) could be shown for medical initial status, e.g., for MQO (IV_{MQO}) upon admission ($\eta_p^2 = .031$). Less daily physical activity (PA) was associated with a poor medical status (see Figure 12). The correlation between the factor PA with medical indicators at admission was observed for all medical indicators (see 'initial state' in Table 18).

[4] The specification of *p*-values is only specified in borderline cases (if not explicitly stated $p < .001$).

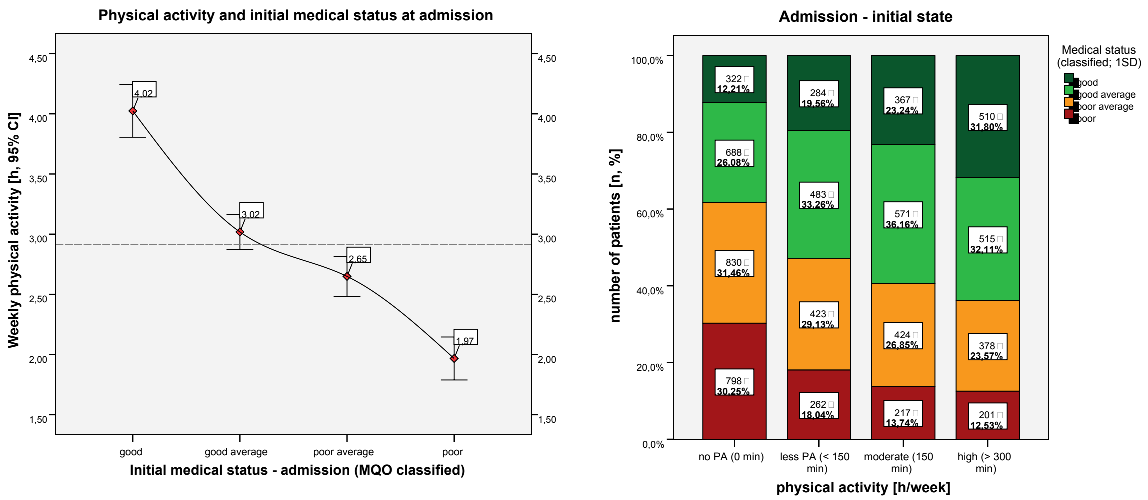

Figure 12: Physical activity and medical status at admission.

Patients reported physical activity (PA) of about 2.91 ± 3.85 hours per week before starting their inpatient stay, and 36.3% of all patients were not physically active at all. There was a strong dependence of baseline medical condition on physical activity (r = -.19; η_p^2 = .031), indicating that patients with no or less physical activity had a poor health status.

Unspecific and indication-specific outcome data clearly demonstrated the success of the program during the inpatient health-care stay, whereby overall medical quality outcomes (MQO_{idx}: η_p^2 = .637), e.g., subjective complaints (MED3: η_p^2 = .701) improved markedly over the three-week period (Table 18).

As shown in Figure 12 and Table 18, a lower daily PA was associated with a poor medical status at the time of admission. From the beginning of the health care program up until the end, PA in leisure time increased by 6.59 ± 4.87 hours per week (η_p^2 = .653). We also detected the moderating effect of (initial) PA on the medical outcome (success) of the health program, but found it to be negligible (interaction): Patients who had been less physical active altered their PA noticeably (time x activity: η_p^2 = .115) and had slightly more pronounced improvements in MQO_{idx} (η_p^2 = .003; see Table 18), which seemed to be mainly caused by better improvements in subjective complaints (MED3). The correlation between the PA before and at the end of the program was low (*r* = .242).

Overall, short-term improvements were clearly visible in all factors and for all subgroups. Sex, BMI and especially initial values had moderate influences on the outcome; the health care program was equally effective for nearly every patient, depending on the overall medical outcome.

Table 18: Summarized medical quality outcome and physical activity before admission.

Aggregated medical outcome factors (UHI and ISI) showed that the program was clearly successful during the health care stay for 86.3% of patients. The medical initial states clearly differed according to different amounts of physical activity in all medical indicators, but not for changes due to the inpatient health care program (GVA). The averaged unspecific and specific indices were of comparable magnitude.

MQO: Medical Quality Outcome - inpatient health care program

[%]	physical activity*	initial state**	better	equal	worse	Ø-improvement***
	0 min	-5.86	22.1	77.0	1.0	2.41 ± 4.21
	< 150 min	2.97	17.6	81.4	1.0	2.41 ± 4.16
MED1	150–300 min	5.76	17.7	81.4	0.9	2.66 ± 4.46
	> 300 min	6.97	18.5	80.7	0.7	2.64 ± 4.25
Shape (BMI, WC)		**1.26**	**19.4**	**79.7**	**0.9**	**MED1: 2.52 ± 4.27**
	0 min	-2.97	56.6	14.3	29.1	11.25 ± 32.06
	< 150 min	1.92	55.1	14.2	30.7	10.63 ± 32.88
MED2	150–300 min	2.16	56.0	15.4	28.6	10.60 ± 31.81
	> 300 min	3.27	53.2	15.8	30.9	9.59 ± 32.14
Cardiovascular (RR, RP)		**0.49**	**55.5**	**14.7**	**29.8**	**MED2: 10.62 ± 32.19**
	0 min	-6.63	93.8	4.7	1.5	33.21 ± 21.59
	< 150 min	1.88	93.5	5.2	1.3	32.23 ± 20.56
MED3	150–300 min	4.01	91.8	7.0	1.2	31.46 ± 20.55
	> 300 min	6.09	90.3	8.6	1.1	30.01 ± 21.69
Subjective (VAS, EQ-VAS)		**0.18**	**92.3**	**6.3**	**1.4**	**MED3: 31.93 ± 21.22**

WC … waist circumference; RR … blood pressure sys./dia.; RP … resting heart rate; VAS … Visual Analogue Scale; EQ-VAS… self-rated health.

[%]	physical activity*	initial state**	better	equal	worse	Ø-improvement***
	0 min	-8.03	81.3	12.0	6.7	*23.03 ± 20.44*
unspecific	**< 150 min**	3.31	79.8	13.2	7.1	*21.91 ± 20.51*
(MED1–3)	**150–300 min**	5.69	80.6	12.5	6.8	*22.01 ± 20.46*
	> 300 min	7.64	78.4	13.5	8.1	*21.07 ± 20.16*
Unspecific Health Index (UHI)		**0.67**	**80.1**	**12.8**	**7.1**	***UHI: 22.15 ± 20.41***

[%]	physical activity*	initial state**	better	equal	worse	Ø-improvement***
overall	**0 min**	-8.39	87.1	9.4	3.4	*23.67 ± 17.92*
MQO$_{idx}$	**< 150 min**	1.55	86.8	10.7	2.5	*23.19 ± 17.05*
(UHI and ISI)	**150–300 min**	5.60	85.7	10.9	3.4	*22.95 ± 17.75*
	> 300 min	9.68	85.3	11.6	3.1	*21.03 ± 17.62*
Medical Quality Outcome		**0.62**	**86.3**	**10.6**	**3.2**	***MQO$_{Index}$: 22.84 ± 17.67***

[%]	physical activity*	initial state**	better	equal	worse	Ø-improvement***
	0 min	-4.66	77.0	19.0	4.0	*12.02 ± 12.19*
disease-specific	**< 150 min**	-2.00	56.6	39.8	3.6	*11.99 ± 11.6*
(MED4, MED5)	**150–300 min**	1.53	64.8	31.3	3.9	*12.29 ± 12.46*
	> 300 min	5.63	70.5	22.4	7.1	*11.42 ± 12.53*
Indication Specific Index (ISI)		**-0.47**	**81.6**	**17.1**	**1.3**	***ISI: 11.94 ± 12.21***

[%]	physical activity*	initial state**	better	equal	worse	Ø-improvement***
	0 min	-4.74	54.9	44.6	0.5	10.57 ± 10.00
	< 150 min	-2.64	56.1	43.6	0.3	10.65 ± 8.81
MED4	150–300 min	0.74	55.3	44.1	0.5	10.79 ± 10.25
	> 300 min	5.45	53.2	46.0	0.8	9.62 ± 10.33
Performance (ergometer)		**-0.85**	**54.8**	**44.6**	**0.5**	**MED4: 10.42 ± 9.91**
	0 min	-1.63	42.9	54.2	2.9	15.56 ± 22.69
	< 150 min	3.65	37.7	59.4	2.9	13.66 ± 22.08
MED5	150–300 min	6.45	36.6	62.0	1.5	13.58 ± 20.68
	> 300 min	6.05	38.2	60.0	1.8	14.40 ± 21.43
ADL (EQ5D)		**3.54**	**38.9**	**58.8**	**2.3**	**MED5: 14.35 ± 21.74**

The threshold for classification (better, equal, worse) is set by a z-difference 0.00 ± 0.20 (= equal).

**. Physical activity before admission to inpatient health care program (h per week).*

***. Initial state at the beginning of health care for monocentric data from the study center. A negative percentile corresponds to a below-average (worse) value in the sample.*

****. Average improvement (percentile) admission–discharge. N = 7,488 I 48.99 ± 6.15 years I 53.7% female, 46.3% male.*

Sustainability[5]

A follow-up survey of a random subsample [n = 532 (46% from N = 1,157)] of patients who had visited a GVA in the last 12 to 16 months was done in September/October 2019. The response rate for the written follow-up survey was 31.6% (n = 168). Numeric medical indicators (cf. Table 2) like VAS, EQ-VAS (MED3), ADL (MED5), as well as weight (BMI; MED1), lifestyle factors (e.g., PA), sick leaves and work activity were subjectively assessed. In addition to patient-reported outcomes, the satisfaction and personal sustainability of the health program were retrospectively questioned.

Responders had had significant better medical initial values in MED3, MED4, MED5 (p < .05; multivariate $_{MED1–5}$: p = .068, η_p^2 = .020; MQO_{idx}: p = .002; percentile difference: 7.10; 95% CI [2.11,12.09]) and seemed physical more active than non-responders (mean difference ~ 0.5 h [0.0, 1.1]; p = .062, η_p^2 = .007), but were representative according to sex (p = .14), diagnosis (p = .21) and age (p = .21). No significant interactions were identified between the response rate and short-term success rates (changes) due to the inpatient health program (all $p_{univariate}$ > .33; $p_{multivariate}$ = .804, η_p^2 = .005).

The physical activity returned to the extent at the beginning of the GVA, around 3.50 ± 2.70 h in the follow-up, whereas the proportion of patients with absolute no PA in the subsample decreased from 16% to 6% (p < .01). A correlation was observed between PA before and one year after the health program (r = .327).

Sustainable effects compared to admission of GVA and around one year later were clearly visible ($p_{multivariate}$ = .001, η_p^2 = .113). Subjective complaints (MED3: $p_{univariate}$ = .015, η_p^2 = .041) were reduced, and shape indicators (BMI: $p_{univariate}$ < .001, η_p^2 = .094) were still better than before the program; significant, long-lasting, positive changes in ADL were not observed (MED5: $p_{univariate}$ = .204, η_p^2 = .011). Compared to the medical outcome at the end of the program, a significant deterioration after one year was observed in MED3 (η_p^2 = .304) and MED5 (η_p^2 = .152), with exception of the BMI (η_p^2 = .043), which slightly further improved. The observed moderating role of PA on current medical health status before the health care program (covariate PA: η_p^2 = .067 at the time of recording; η_p^2 = .049 at the end of inpatient health care) disappears one year later, by which time the patients had returned to their everyday lives (covariate PA: η_p^2 = .007 at the one year end point). Nevertheless, PA before admission was a main (between) factor between subjects for an estimation of medical indicators over the time-course ($p_{multivariate}$ = .019; η_p^2 = .047) beside initial state ($p_{multivariate}$ = .000; η_p^2 = .186) it had been the best predictor for prognosis. Only the BMI showed

[5] Not published yet;

a significant interaction over time in MED5, as obese patients had a higher risk of relapse or even a deterioration in their ADL below the level of baseline values after one year ($p_{univariate}$ = .005; η_p^2 = .051).

Of the post survey sample, 89.5% were gainfully employed one year after the health program, and only 4.6% were unemployed. This was broadly in line with the job situation before the health program (six patients had been retired after GVA). For the last 12 months, 50.6% had taken sick leave for about two weeks on average, which roughly corresponds to the average in the population (165). At the time of the post survey, 5.6% had taken sick leave. The reported pain at work was still high with a mean 3.12 ± 2.95 (VAS: 0–10), and only 29.1% of the patients reported that they were free of pain (VAS ≤ 1). Three-quarters of the respondents stated that they wanted to stay active in their profession, around 10% were undecided, and ~10% of the subsample had already retired before entering the GVA. On a VAS of 0 to 10, the GVA was regarded as a necessary proof (9.24 ± 1.48; MED = 10) that could sustainably improve their ability to work (6.69 ± 2.91; MED = 8) and lifestyle (6.25 ± 2.80; MED = 7). Among the participants, 77.6% were 'very satisfied' and 18.4% were 'satisfied' with the inpatient program. In particular, active treatments were seen as a guarantor of success (9.29 ± 1.39, MED = 10; VAS: 0–10), followed by passive treatments (8.77 ± 1.69, MED = 9.50) and lectures or workshops (6.96 ± 2.74, MED = 7.65).

4. Discussion

In times of dwindling resources, it is becoming increasingly important to justify medical effectiveness for practical and health reasons. Constantly changing framework conditions present challenges for quality assurance management, for which structural, process and outcome characteristics are used to evaluate the degree to which predefined goals have been achieved.

Our data show that a majority of the patients included in our studies clearly benefited from inpatient rehabilitation, independent of their indications, diagnoses and ages. Improvements in unspecific and indication-specific outcome indicators were similar for all patients. These study findings have shown that unspecific and disease-specific outcomes behave differently. They also show that the timing of post-acute rehabilitation plays an important role in disease-specific but not in unspecific health changes.

The selection of outcome indicators needs to take into account evidence-based and economic considerations to guarantee a comparable standard of quality medical treatment. Indication-specific indicators are central to rehabilitative treatment and restore the patient's ability to work or reintegrate into the social and professional environments. This score cannot be effectively compared between indications because different medical parameters are used for medical assessment, but it can be used to evaluate general relationships with relevant factors that influence the healing and recovery process.

Another focus is placed on unspecific health features, such as obesity, blood pressure and physical inactivity. Physical activity was identified as a major factor influencing the observed medical health status. These unspecific characteristics are associated with poorer health, cardiovascular disease and metabolic disorders (41, 43, 166). They are among the most important risk factors for chronic diseases and premature death (167). In addition to determining the individual, symptomatic treatment of a patient, an important task in inpatient rehabilitation is to sustainably reduce these risk factors. Quality of life and functioning are characterized by positive lifestyle modifications, e.g., an increase in physical activity. Accordingly, a reduction in the recorded unspecific health indicators, such as BMI (168), waist circumference, blood pressure, heart rate and pain, is also highly relevant for the inpatient rehabilitation and health care of patients with different diagnoses and indications.

The inpatient health care program (GVA), therefore, also prioritizes active treatments like physical exercise and medical training, as most of the patients are overweight, have high blood pressure and are physically inactive. The findings of our study underline the fact that the lack of exercise is one of the biggest problems facing members of our society (169).

These characteristics are associated with poor health, cardiovascular diseases, cancer and metabolic disorders. They are among the most important variable risk factors for chronic diseases and premature death (170). Health care professionals who provide individual symptomatic treatment for patient on inpatient wards are also given the important task of sustainably reducing these risk factors. Quality of life and functioning are characterized by positive lifestyle modifications, such as an increase in physical activity. Therefore, an observed reduction in the recorded basic clinical parameters, such as BMI, waist circumference, blood pressure and pain (171, 172), is highly relevant when providing inpatient health care of different diagnoses (173, 174).

In order to work meaningfully and deductively, it is helpful to reduce the abundance of partially redundant information to a manageable, uniform level. These key figures of UHI, ISI and overall MQO_{idx} provide simple and quick overviews of the "unspecific" and "specific" effectiveness of the rehabilitative stay for certain treatment programs.

4.1 Medical Quality Outcomes - Unspecific vs. Specific Quality of Outcomes

When assessing the effectiveness of inpatient rehabilitation based on the nonspecific features of the health outcome, it is not as important to differentiate between medical indications, as effect sizes are similar. Sex and age are also of minor importance. If unspecific health indicators at discharge are compared with the initial medical evaluation data, we observe that 71.4% of patients benefited directly from inpatient rehabilitation (Table 11). Significant interactions with further grouping features can be classified as "small" compared to the main effect time (rehabilitation). Therefore, the observed strong rehabilitation effect was similar among all subgroups, because medical treatments and exercise seemed to work equally well for nearly all patients. We predict that this unspecific success could occur during all inpatient rehabilitation stays and programs due to the provision of a series of regular therapeutic stimuli, exercise training as well as recovery periods over a defined period, as is the preventive effect of physical activity in this environment. These would potentially lead to functional adaptation, which is characterized by improvements in regulatory qualities and the economization and normalization of physiological functions. Changes of unspecific health outcomes are independent of the delay between medical treatment (surgery) and rehabilitation (Figure 8). In an untreated control group without rehabilitation, therefore, no positive spontaneous change in the constitutional state of health would be expected.

Unlike unspecific health scores, our findings indicate that the moderating factors play more important roles in the specific outcome quality. Older patients (> 60 years) showed an equal or even more favorable rehabilitation outcome than other patients, especially with regard to symptom-specific indicators (Figure 6, Table 13). As the nature and severity of the underlying disease influences the outcome, it is not surprising that the relationship between age and outcome was not the same (e.g., in all indications; cf. Figure 7). One interesting finding of this literature review is that older orthopedic and cardiovascular patients obtained the largest benefit in terms of overall medical quality outcome (131). To our knowledge, this is the first time this benefit has been observed in orthopedic patients.

According to our results, inpatient rehabilitation should start as early as possible to achieve favorable disease-specific outcomes. In particular, patients who entered Phase II earlier (< 6 weeks) after undergoing surgery and patients with poorer initial medical evaluations showed better success as measured by their symptom-specific characteristics (75, 76).

For example, for the health care program (GVA), our data and results demonstrate that the medical initial status was the most important main factor identified between subjects, allowing an estimation of medical indicators over the time-course ($\eta_p^2{}_{\text{ multivariate}} = .270$). Therefore, this factor was the best predictor for prognosis. A mathematical and inherent dependence naturally exists between the initial values and their changes (interaction). Poor initial values correlate with better medical outcomes, but their influence differs between medical indicators. Thus, cardiovascular indicators (MED2) strongly improved in patients with poor initial states, whereas a strikingly low correlation could be observed between physical performance indicators (MED4). Other important determinants of the health status identified were sex, BMI and PA. PA was associated with poor medical status (Figure 12). We observed that sex and BMI affected the medical outcome (success) differently and played moderating roles. Men were more frequently affected and showed better results in terms of obesity and hypertension, while women showed slightly more improvements with regard to their reported major complaints (MED3). Taking into account the different initial values (IV_{MQO}) used for women and men as covariates, sex still influenced the results or even emerged as a primary determinant (time x group: $\eta_p^2{}_{\text{ multivariate}} = .072$). In general, male patients responded better to the program. These results indicate that gender-specific considerations need to be made in health prevention programs and treatments. Beside a better physical performance, obese patients initially had poorer baseline scores, but their cardiovascular indicators developed significantly better over the short-term than those with normal weight. This interaction effect (MED2: $\eta_p^2 = .010$) disappears when the different initial values are taken into account ($\eta_p^2 = .001$).

These findings underline the importance of taking a multidimensional view of specific and unspecific outcome quality and describing two independent components of rehabilitation. A multidisciplinary rehabilitation or GVA is based on the reduction of risk factors (primary and secondary prevention, unspecific indicators), an increase in fitness (167) and a specific medical treatment of the symptoms (tertiary prevention, specific indicators).

The most pronounced effects of inpatient rehabilitation could be seen for the parameters of subjective complaints and indication-specific index. More than two-thirds of the patients experienced significant improvements regarding symptoms and specific characteristics.
However, 24.8% did not show significant changes, and 4.7% showed symptoms and specific characteristics that worsened from the beginning to the end of rehabilitation (Table 11). Therefore, our findings indicate that not all patients can directly benefit from this treatment. Overall (MQO_{idx}), rehabilitation therapy leads to improvement in the vast majority of patients (77.9%, *z*-difference = 0.48 ± 0.37, d_{Cohen} = -1.22), and the same applies to the health care active program GVA (Table 18).

Patient satisfaction was generally very high (97%) (175) and appears to reflect the structural and process conditions more closely than the professionally assessed health conditions. Due to strong ceiling effects, the patient satisfaction cannot be used to make a differentiated consideration of the medical outcome quality (cf. e.g., Outpatient Phase III Cardiac Rehabilitation, p.46).

4.2 Applicability to Rehabilitative Clinical Practice

Despite the large international differences in the kinds of rehabilitative health care teams and treatment measures, the observed effect sizes can support individual evaluations. It is also important to consider the medical focus, the rehabilitative practice and performance profiles, as documented outcomes depend on different treatment programs and the associated uses of health care resources. The absolute values and individual profiles of the medical quality outcome should always be evaluated according to the given setting and at the doctor's discretion. Single measurements are subject to a variety of moderating influences and measurement errors. The presented continuous measures of MQO_{idx}, therefore, have advantages in terms of their (scale) properties and sensitivity to frequently applied categorical criteria. When using the presented clinical values of the MQO_{idx}, the monocentric character of the work has to be considered.
Due to the prescribed performance profiles and fact that assignment modalities are centrally controlled by the insurers, however, we can assume that the initial values presented and especially the changes in the MQO are representative of the inpatient rehabilitation setting in Austria. Different individual baseline values must always be taken into account, as poorer outcome parameters at the beginning of rehabilitation are accompanied by a greater potential for improvement, which, of course, is statistically given if difference values (post - pre) are applied (e.g., for rehabilitation: MQO_{idx}: $r_{\text{pre vs. post-pre}}$ = -.44; for GVA: r_{MQO} = -.36).

The presented results suggest that the expected rehabilitation effects on the medical quality outcome are universal. A more detailed characterization of non-responders still needs to be made.

4.3 Limitations

The practical significance of the Medical Quality Outcome or relationships with external criteria (endpoints), such as the incapacity for work, still needs to be investigated. To further develop research in this direction, it may be helpful to perform a global evaluation between medical outcome factors and socio-medical relevant external criteria. Closer networking, the exchange between responsible institutions and more transparency would be desirable. The objectives and questions presented in this thesis (cf. p.18) are of great importance for our health care system.

It is still necessary to clarify which observed changes in medical outcome factors are significant to the sustainability of rehabilitative measures and to what extent optimized treatment pathways can influence these. The beneficial effects resulting from participation in a rehabilitation or inpatient health care program for well-being may not be sustainable once the patients return to their usual everyday lives. Improvements in terms of one outcome may well be accompanied by the deterioration of other outcomes. For this reason, most researchers do not expect such programs to make lasting changes in the patient's lifestyle (176). However, even minor changes in lifestyle and physical activity have a positive effects on healing, lead to functional adaptations and normalization of physiological functions and help the patient to recover from chronic inflammatory or degenerative diseases (4, 146, 177). Future research will be carried out to clarify the length of the impact of an inpatient health program, even if lifestyle changes are not made, and determine what further support is needed to optimize treatment pathways and sustainability.

One limiting factor is the lack of physical activity or cardiorespiratory fitness markers, which have not yet been included in routine measurements (4, 156, 178, 179). Therefore, multidimensional approaches to quality outcomes should be taken.

4.4 Conclusion

This summary of information from relevant papers shows for the first time that specific and unspecific health indicators behave differently during the time-delay between surgery and inpatient medical rehabilitation. Whereas specific health indicators improve, unspecific health indicators deteriorate over time, if the patients are not treated in a rehabilitation program.

To evaluate the quality of medical outcomes, health care professionals use the usual "primary patient-oriented" assessment methods. They can also collect self-report questionnaires from patients who perform subjective self-assessment and express their satisfaction with treatments and programs. In addition, they can examine quality registers to extract patient information regarding surgical frequencies, lengths of stay and complications. The medical indicators described in this work, however, represent valuable complements to the currently accepted methods used to assess the quality of medical outcomes.

To our knowledge, no previous research has been conducted on individual medical indicators for inpatient rehabilitation and prevention programs with this sample size. The cumulative findings presented in this dissertation are essential in that they allow medical professionals and researchers to compare health programs and developments in prevention, health care and rehabilitation, more effectively enabling them to improve the well-being of patients.

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6. Appendix 1

6.1 Author Contributions

Vincent Grote (VG) was significantly involved in the conception, design, data acquisition, data analysis and interpretation. He wrote the manuscripts and released the final versions for publication. He takes responsibility for the accuracy and integrity of all aspects of this research.

Table 19: Contributions to published and submitted research articles of the candidate.

		%
CONCEPT	the idea for the research or article, framing the hypothesis	90
DESIGN	planning the methods to generate results	95
SUPERVISION	oversight and responsibility for the organization and course of the project and the manuscript	95
RESOURCES	euros, equipment, space, personnel vital to the project	15
MATERIAL	biological materials, reagents, referred patients	5
DATA COLLECTION/PROCESSING	responsibility for doing experiments, managing patients, organizing and reporting data	50
ANALYSIS/INTERPRETATION	responsibility for making sense of and presenting the results	95
LITERATURE SEARCH	responsibility for this necessary function	70
WRITING	responsibility for creating all or a substantive part of the manuscript	95
CRITICAL REVIEW	reworking the manuscript for intellectual content before submission, not just spelling and grammar checking	50

6.2 Conflicts of Interest

The author (VG) declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. VG has written this thesis during a period of educational leave from the Medical University of Graz. VG previously worked at Humanomed Consult GmbH, which runs the clinical trial center (Humanomed Center Althofen, Austria).

6.3 Original Contributions

Some of the original contributions are open access contributions (3, 4):

Citation (3): Open access peer-reviewed chapter - PDF file with 27 pages

Grote, V., Unger, A., Puff, H., Böttcher, E. What to Expect: Medical Quality Outcomes and Achievements of a Multidisciplinary Inpatient Musculoskeletal System Rehabilitation. In: Bernardo-Filho M, Sá-Caputo D, Taiar R, editors. Physical Therapy Effectiveness [Working Title]: IntechOpen; 2019, online first. p. 27. doi:10.5772/intechopen.89596

Citation (4): Open access version - PDF file with 12 pages

Grote, V., Levnajic, Z., Puff, H., Ohland, T., Goswami, N., Fruhwirth, M., Moser, M. (2019). Dynamics of Vagal Activity Due to Surgery and Subsequent Rehabilitation. Front Neurosci, 13(1116). doi:10.3389/fnins.2019.01116

Original conference contributions and copies of presentations or posters are not fully presented within this thesis (cf. 5), some are not quotable. You can find them at the following URL: https://www.researchgate.net/project/Rehabilitation-and-Health *(Date Accessed: 2020-02-07)* as well as all work and contributions on the topic of this cumulative dissertation.

6.3.1 Released Publications without Public Access

The following personal manuscripts (1, 2) were published in "Phys Med Rehab Kuror" of the copyright holder "Georg Thieme Verlag KG". Phys Med Rehab Kuror is a RoMEO blue journal, which allows archiving final drafts post-refereeing (Green Open Access). For the accepted versions of the manuscripts, see Appendix 2.

Citation (1): Accepted author's version of manuscript - PDF file with 20 pages (in German)

Grote, V., Böttcher, E., Zahirovic, S., Moser, M., Puff, H. (2018). Vibration Therapy in Orthopaedic Rehabilitation - Evaluation of in-Patient Rehabilitation Measures in Orthopaedic Patients Using a Mechanical Vibration Couch. Phys Med Rehab Kuror, 28(03), 171-183. DOI: 10.1055/a-0584-0168

Citation (2): Accepted author's version of manuscript - PDF file with 36 pages (in German)

Grote, V., Böttcher, E., Mur, E., Kullich, W., Puff, H. (2019). Medical Quality Outcomes: Unspecific Outcome Parameters of an Inpatient Musculoskeletal System Rehabilitation in Austria. Phys Med Rehab Kuror, 29(02), 104-117. DOI: 10.1055/a-0835-6481

6.3.2 Submitted Manuscripts

The submissions of draft manuscripts are presented within this thesis (see Table 10 f. and Table 17 f.).

Submission A:

Grote, V., Unger, A., Böttcher, E., Muntean, M., Puff, H., Marktl, W., Mur, E., Kullich, W., Holasek, S., Hofmann, P., Lackner, H.K., Goswami, N., Moser, M. Health and Disease-Specific Indicators React Differently to Inpatient Medical Rehabilitation - A Non-Randomized Controlled Routine Outcome Study in a Sample of over 16,000 Patients. Submitted 26/12/2019.

Submission B:

Grote, V., Unger, A., Hofmann, P., Marktl, W., Holasek, S., Moser, M., Böttcher, E. An Inpatient Health Care Program for Musculoskeletal Disorders to Improve Well-being in Patients with Chronic Conditions. Submitted 13/12/2019.

Appendix 2 – Additional PDF Files

PDF files

(cf. 6.3 Original Contributions, p.71)

Provisional chapter

What to Expect: Medical Quality Outcomes and Achievements of a Multidisciplinary Inpatient Musculoskeletal System Rehabilitation

Vincent Grote, Alexandra Unger, Henry Puff and Elke Böttcher

Additional information is available at the end of the chapter

Abstract

The incidence of chronic diseases is rising. Rehabilitation plays a vital role in preventing and minimizing the functional limitations associated with chronic conditions and aging. Routine outcome measures include disease-specific and unspecific general health parameters. This study evaluates indicators for medical quality outcomes from 10,373 patients (61.00 ± 13.65 years, 51.7% women) who have undergone orthopedic rehabilitation for three weeks. Inpatient rehabilitation reduces lifestyle-related risk factors, optimizes organ functioning and improves the well-being in the majority of patients (81.3%; SMD = 0.52 ± 0.38). Improvements of unspecific and indication specific outcome parameters can be observed in a comparable magnitude. However, disease specific and unspecific health factors are not directly related to each other (r = 0.19). Age, gender, ICD-classification and time of rehabilitation have an influence on initial values and on indication-specific medical outcomes but are insignificant with regards to improvements in unspecific medical outcome parameters. Inpatient rehabilitation includes two main pathways of medical practice, which can be clearly distinguished in terms of their therapeutic outcome. There are general health interventions, such as lifestyle modifications, diet and physical exercise, and symptom-specific treatments. So multidisciplinary medical rehabilitation improves general well-being and physical functioning as well as reduces risk factors in the majority of patients.

Keywords: inpatient rehabilitation, medical quality outcomes, routine outcome measurement, reference data, rehab success

1. Introduction

The definition of rehabilitation has become more transparent all over the world after the World Health Organization (WHO) published the five health strategies (promotion, prevention, cure, rehabilitation and palliative care) in rehabilitation [1]. Rehabilitation was previously understood as a heterogeneous approach. It was framed as a highly specialized service for athletes, a controlled training intervention or a post-injury service for return-to-work intervention. The definition was standardized through the WHO to a homogenous understanding of rehabilitation as a service to restore functioning, ameliorate the impact of the reduction in capacity and minimize further initial health problems in all stages of health provision [2].

Special care in rehabilitation is given to the ailments of the modern society. As such, especially risk factors like sedentary behavior[1], physical inactivity, overeating causing obesity, alcohol abuse and smoking leading to various chronic diseases that immediately affect the musculoskeletal system [3] are causes for concern. Due to those lifestyle choices that lead to potentially life-threatening conditions, physical activity has become an important therapeutic approach. It is a primary, secondary or tertiary therapeutic approach of chronic diseases over the last decades. Physical activity recommendations are now broadly understood as health-related interventions that propose a minimum dose of physical activity.

The WHO [1] suggests at least 150 minutes of moderate aerobic activity or 75 minutes of vigorous aerobic activity throughout the week for adults. In addition, muscle-strengthening activities should be done involving major muscle groups on two or more days a week and sedentary behavior should be reduced. Small amounts of physical activity already have a positive impact on the health status; however, the strongest effect can be observed in adults that transformed from an inactive to an active lifestyle [4–6].

Medical intervention programs therefore do not only aim to restore physiological functioning, reverse or undo the damage caused by disease or injury, but also rather to optimize the health status by improving strength and aerobic capacity. The amelioration of the physical constitution leads to health-promoting effects like the reduction of high blood pressure, a better glucose profile and reduced blood lipids [7, 8]. Physical activity has a positive impact not only on metabolic and cardiovascular diseases but also on the musculoskeletal system.

Complaints of the musculoskeletal system are most commonly those of inflammatory and degenerative origin. These origins of disease are the cause for chronic pain, painful functional impairment and a reduced quality of life worldwide. Rheumatoid arthritis is found in 3.2% of women and 1.9% of men. Furthermore, another increasing ailment is osteoporosis, which is found in 3.1% of women and 1.9% of men, with a high prevalence from the age of 80 onwards [9].

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[1]For example, through (screen) workplaces and automation, leisure activities such as video games, social media and television.

The most common symptom of the musculoskeletal system is back pain (60–80% long-time prevalence [10, 11]). The prevalence is dependent on age, with a rise of prevalence with age. The highest prevalence for back pain is set between 40 and 69 years; women are more affected than men [12, 13].

The findings of an analysis by the Austrian Health Survey 2014 [14] report an estimated rate of 24% (about 1.8 Mio individuals) suffering from chronic back pain. Furthermore, 19% claimed about discomfort of the cervical spine. The cervical spine complaint was gender dependent (23% women versus 14% men). Arthrosis was found in 15% of women and 8% of men. The gender difference refers not only to the frequency of the disease but also to the pain perception, due to a higher rate of female pain sensitivity, lower threshold for pain and a lower suspension of pain [15].

Due to the high prevalence of degenerative diseases of the musculoskeletal system, there is also a demand for surgical treatment with endoprosthesis material. The highest operative treatment rates for such procedures worldwide are found in Switzerland, Germany and Austria. In Germany, about 230,000 hip, 170,000 knee and 25,000 shoulder endoprosthesis surgeries were performed in the year 2011 alone [16].

Physiotherapy and physical activity are fundamental components for the process of recovery. The body of available knowledge confirms positive effects of physiotherapy and physical activity throughout all organ systems. It reduces swelling as well as promotes building strength and aerobic capacity. Through the process of physiotherapy and physical activity interventions, a total physiological functionality after surgical treatment can be achieved. Moderate physical activity reduces the risk of osteoporosis and improves the osseointegration of bone substitutes. Almost all musculoskeletal diseases can be treated by therapies including physical activity and strengthening programs [17–20]. Physical activity thus has become the gold standard among medical treatments.

1.1. Orthopedic rehabilitation

Following the WHO definition, the rehabilitative process can be divided into four phases: phase I includes the early mobilization in primary treatment, phase II provides follow-up treatments or post-acute therapy in rehabilitation centers, phase III tries to integrate and stabilize the long-term life modifications and phase IV deals with long-term rehabilitation including a probably outpatient aftercare. The aim of orthopedic inpatient rehabilitation (phase II) is to restore the health status based on the bio-psycho-social health model.

1.1.1. Situation in Austria

Musculoskeletal diseases, caused by inflammatory, degenerative processes or injuries, permit an inpatient orthopedic rehabilitation (WHO, Phase II [21, 22]) over 3–4 weeks for restoring physiological functioning and reintegrating to social and professional life.

Based on historical decisions [23] and Health Technology Assessments (HTA) (e.g., [24]), there is currently a framework of contracts with the federal Austrian social security institutions entities in place[2]. This includes performance agreements for orthopedic rehabilitation (see [25]), based on criteria regarding the quality of processes and treatment outcomes [21]. Criteria include individual detailed results that demand a standardized statistical recording of outcome parameters from admission up to discharge of the rehabilitation program. Furthermore, evaluation and statistical analyses of these medical outcomes are generally not open to the public [26].

1.1.2. Implementation of orthopedic rehabilitation in Austria

There is strong evidence that rehabilitation is necessary as part of the treatments for inflammatory or degenerative diseases, as well as for postoperative conditions or injuries of the musculoskeletal system. The underlying condition's severity and expectancy of the restoration of physical function are requirements for obtaining an inpatient orthopedic rehabilitation. For patients affected by musculoskeletal disease, medical treatment and a large range of rehabilitative treatments are available. The inpatient treatment lasts on average 2–3 hours per day. An individual rehabilitative program consisting of active and passive treatments is provided (see **Table 1**). Active treatments consist of physical activity including gymnastic and individual physiotherapy sessions and the medical training focuses on underwater , ergometer , Nordic walking , strength , balance , relaxation and motion training. Passive treatments contain sessions like massages, thermotherapy, electrotherapy, ultrasound and educational lessons like various lectures, or psychological coaching. Each patient is offered a program of at least 1800 therapy minutes during 3 weeks, split up into approximately 50% active and 50% passive treatments that highly surpass the physical activity guidelines of the WHO (150 minutes workout in moderate intensity and strengthening exercise twice a week).

	Physical exercise	**Medical training**	
Active	Gymnastic	Underwater gym	Appro×. 50%
	Individual physiotherapy	Ergometer training	
	Sensomotoric training	Strength training	
	…	Balance & function training	
	(Passive) **Treatments**	**Education**	
Passive	Massages	Health-related talks and trainings	Appro×. 50%
	Thermotherapy	Psychological	
	Electrotherapy	Coaching	
	Ultrasound	…	
Required total amount		At least 1800 minutes (within 3 weeks)	

Table 1. Quantity and type of therapies over three weeks.

[2]In particular the pension insurance institution.

Medical rehabilitation is structured in different ways all over the world, although a tendency for a standardization of the social and health system can be observed. In Germany and Austria, the social insurance offers inpatient orthopedic rehabilitation over a period of 3–4 weeks in specialized rehabilitation centers with an interdisciplinary team. Some other countries only provide outpatient rehabilitation [27].

1.2. Efficacy and sustainability of orthopedic rehabilitation

Diseases demand a certain continuity of the therapeutic process for success after rehabilitation. This means that rehabilitative programs should focus not only on physical activity programs during the stay but also on sustainability of physical activity after the rehabilitation. Therefore, an inpatient stay should also lead to a health-related modification in lifestyle. The efficacy of inpatient rehabilitative programs and especially their sustainability over a long period are important research issues. Literature shows that during the rehabilitative stay, pain can be significantly reduced, and a long-term improvement of physiological functionality can be achieved. The success can be measured even after 12–21 months after rehabilitation [28, 29].

The fact remains that physical activity programs have a positive impact on the physiological performance of patients. However, the dropout rate for long-life active and health-related lifestyle change maintenance is high. Findings support the sustained efficacy of an intense, multimodal orthopedic rehabilitation, with moderate evidence, including an improved subjective health status and reduced pain [30]. For rehabilitation treatment after hip and knee endoprosthesis (TEP) [31–34] and chronic back pain [35–37], a level of evidence Ia/Ib is stated. The combination of physiological and psychological training significantly leads to positive changes [18, 38, 39]. The data confirm that a combination of physical activity and psychosocial training-based treatments has an influence on pain reduction and mental well-being.

Studies in other countries state that about 57% of patients in Europe and even 70% of patients in the US are able to restart regular full-time work and show significant improvements of psychosocial, physiological parameters after inpatient rehabilitation [40–43]. An interdisciplinary treatment of medical, physical activity based and psychological therapy ensures a high return to professional life [44, 45].

2. Methods

The medical outcome parameters required by the performance profile of the federal Austrian social security institutions involved in quantifying the quality of rehabilitation outcomes are the basis of this work. We provide descriptive standardized numeric indicators of the rehabilitation process as well as monocentric reference data for a 3-week inpatient orthopedic rehabilitation program. Data collection was performed by doctors and healthcare professionals during routine medical treatment. Standardized clinical characteristics of patients were recorded systematically at the time of admission and discharge. The easily quantifiable medical parameters included general health characteristics such as body measurements and cardiovascular parameters, psychological indicators such as pain and subjective health, as well as specific indicators such as daily activities, motor function and physical performance (see **Table 2**).

These quality-of-outcome measures are to be documented in the discharge report at the beginning and the end of the phase II rehabilitation (this correlates with the methodology of a pre-post comparison). Respectively, data were also summarized using a descriptive evaluation in terms of content and factor analysis. This provides us a simple descriptive evaluation model through independent factors for the sake of a complete evaluation of the outcome quality [26].

2.1. Orthopedic reference sample at the clinical trial center

During the service period from 2016 to 2018, a total of 10,373 patients (61.00 ± 13.65 years, 51.7% women) were enrolled in a specialized interdisciplinary hospital for rehabilitation (Humanomed Center, Austria) (**Table 3**). A categorization of reasons for hospital treatment was based on the admission diagnosis. Reasons for admission were musculoskeletal diseases (M, 85%) or injuries (S, 15%). Categorizations were based on ICD-10. The majority of patients were admitted for rehabilitation due to back pain (29.6%) followed by upper/lower limb joint as well as knee (21.4%), hip (16.3%) and shoulder (12.0%) disorders. About 73.3% of the patients were admitted after surgery (OP)[3]. Just under a half of those patients (42.2%) were treated with an endoprosthesis (EP) (overall, 31.9%). The proportion of EP rehabilitation procedures was 64.7% for knee patients and 84.7% for hip patients. The period between acute care rehabilitation (OP) averaged 8.4 ± 4.0 weeks. However, patients with knee and hip TEP progressed from phase I to phase II earlier (median, 6 weeks)[4].

The average inpatient length of stay was 22.00 ± 2.6 days; 2.2% of all patients discontinued their inpatient treatment prematurely due to a loss of rehabilitation capacity (for example, acute illness) or for private reasons (criterion ≤ 18 treatment days). In 3.8% of the patients, the inpatient stay was 4 weeks.

2.2. Ethical aspects

This study (A retrospective study-Routine Outcome Parameters of an Inpatient Rehabilitation in Austria) was reviewed and approved by an Ethics Committee (Vote by the Ethics Committee of the Medical University of Graz, dated 02.05.2019, EC Protocol Number: 31-321 ex 18/19). Person-related and health-related data were collected as part of routine medical care and quality management at the Humanomed Center Althofen (9330 Althofen, Moorweg 30). Data processing was done according to standard operating procedure by the responsible data processing party: Humanomed Center Althofen GmbH, Data Protection Officer: Mag. Karl Klein, Jesserniggstraße

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[3]Corresponds to a follow-up treatment procedure (AHV), which can be used in Austria for three to four months from the grant date (in Germany within 14 days after discharge Phase I). The remaining patients are a (R) HV [(rehabilitation) treatment], where the time limit is 8 to 12 months.

[4]For knee and hip TEP patients in orthopedic rehabilitation, a quasi-experimental control group (waiting group) results from the different onset times [period between acute care (surgery time) and the beginning of the follow-up treatment procedure (AHV)].

Orthopedic rehabilitation indicators for medical quality outcomes (MQO, [z*])						
Unspecific general health parameters			**Disease-specific health parameters (indication-specific outcomes)**			
MED1	BMI	[kg/m^2]	**ORT1**	Quality of life	EQ-5D	[%]
	Abdominal circumference	[cm]				
	ANATOMY	**[z]**		**ADL** (activities of daily living)		**[z]**
MED2	Blood pressure systolic	[mmHG]	**ORT2**	Motoric function	Roland-Morris	[ ]
	Blood pressure diastolic				WOMAC	[ ]
	Resting heart rate	[bpm]			Constant-Murley	[ ]
	PHYSIOLOGY	**[z]**		**FUNCTION**		**[z]**
MED3	VAS (pain)	[cm; 0–10]	**ORT3**	Walk test	Timed up & go	[sec]
	EQ VAS (self-rated health)	[%; 0–100]			10 m	[sec]
	DISCOMFORT	**[z]**		**PHYSICAL ABILITY**		**[z]**
UH_i	**Unspecific health index** MED1, MED2 & MED3	**[z]**	**SO_i**	**Specific Ortho Index** ORT1, ORT2 & ORT3		**[z]**
MQO	(overall) **Medical quality outcome** UH_i & SO_i					**[z]**

*Standard scores, also called z-values (z), are calculated by subtracting the (population) mean from an individual raw score and then dividing the difference by the (population) standard deviation (here: for all orthopedic patients). As shown in the results section, deviations from zero respectively mean differences of z-values can be interpreted as an effect size (c.f. Cohen’s d).

Table 2. Parameters of medical quality outcomes.

Classification according to ICD-10	Number of patients		Age	Women		Endoprosthesis	
Localization/main diagnosis	**abs.**	**%**	**Mean ± SD**	**abs.**	**%**	**abs.**	**%**
Back (spine)	3067	29.6	57.2 ± 13.3	1509	49.2	12	0.4
M41, M43, M48, M50, M51, M53, M54, S32, S22, S12							
Knee	2220	21.4	64.7 ± 12.5	1225	55.2	1437	64.7
M17, M23, S83							
Hip	1688	16.3	67.1 ± 11.0	928	55.0	1429	84.7
M16							
Shoulder	1249	12.0	57.8 ± 11.3	562	45.0	32	2.6
M75, S42, S43, S46							
Lower leg and thigh	723	7.0	62.1 ± 16.5	414	57.3	103	14.2
S82, S86, S72							
Other arthritis	400	3.9	62.7 ± 13.4	219	54.8	139	34.8
M19, M25							
Other	330	3.2	60.7 ± 14.4	173	52.4	141	42.7
T84, S52, M79, M77, M87, S92, M06							
Other diseases (musculoskeletal system)	696	6.7	55.3 ± 15.4	338	48.6	17	2.4
ICD-10Kat < $n = 20$							
Total	10373	100.0	61.0 ± 13.6	5368	51.7	3310	31.9

Table 3. Sample number of patients undergoing rehabilitation of the musculoskeletal system.

9, 9020 Klagenfurt. The data from the hospital information system upon which the publication is based were compiled in compliance with all regulations of the Austrian Privacy Act and the Declaration of Helsinki in its current version. Data collection was done also in accordance with national legalization (hospital statutes, contracts with insurance-authorized institutions, etc.) through the rational of mainly collecting scientific data in the public interest.

2.3. Medical outcome quality

Medical outcome quality is defined as the "measurable change in the profession-ally assessed state of health, the quality of life and the satisfaction of a patient" (see Austrian Federal Quality of Healthcare Act, GQG). The outcomes become visible by "the difference between the initial state and the state at treatment end" (c.f. [46]).

The outcome measurement in rehabilitation can be based on various methodological approaches, such as questionnaires, performance tests, equipment measurements and functional physical examinations. The outcome quality measurement, "the outcome," includes features on health (e.g., symptoms and pain), functional levels (e.g., performance) and educational levels. In addition to the patient's subjective assessment ("patient-reported outcomes (PRO)"), medical, diagnostic and other relevant outcome measures/criteria (e.g., ICF) are documented by healthcare professionals.

The aim of the present work is to provide a valid basis for routinely assessing the quality of medical outcomes (routine outcome measurement) based on common data acquisition. The focus therefore is on general (nonspecific, body constitution based) and indication-specific parameters. Continuously collected medical reference values have diverse potential benefits in quality assurance, awareness raising, goal setting and decision-making. The data are also important for evaluation of different care models.

2.3.1. Quantifying "medical outcome quality"

In addition to the descriptive analysis of single indicators, the analysis evaluates the effects of inpatient rehabilitation stay and the medical quality outcome (MQO). This is calculated on the basis of representative monocentric normative data (N = 10,373; see **Table 3**). The selection of clinical parameters follows the requirements of federal social security instate in the performance profiles of accredited Austrian institutions for outcome analysis, which should guarantee a comparable medical service quality standard. A success index is calculated by summarizing the compulsory basic clinical data of the patients (see **Table 2** and [26]).

1. The "Unspecific Health Index" is the arithmetic mean of three independent areas of measurement: body measurements (BMI and abdominal circumference), cardiovascular parameters (blood pressure and resting heart rate), discomfort (visual analogue scales (VAS pain, [47]) and subjective health status (EQ-VAS, [48])). These parameters should provide a simple and quick overview of "unspecific" effectiveness of a rehabilitative stay.

2. The "Specific Ortho Index" corresponds to a z-normalized mean of "activities of daily living" (EQ5D), "function" (Roland-Morris, WOMAC or Constant-Murley, depending on the affected body region) and the "physical ability" (walking tests).

The Unspecific Health Index can be interpreted as an indicator of general health status or the current body constitution, whereas the Specific Ortho Index corresponds to a disease-specific health parameter (indication-specific outcome). Both indexes together form the "medical quality outcome" in equal parts.

2.3.2. Statistical methods

Based on the value distributions, the individual outcome parameters were transformed into z-values, which allowed a conversion into percentiles. By means of the z-standardization, different scaled quantities can be summarized and changes can be uniformly quantified [standardized mean differences (SMD)]. A value of 50% (median) or a z-value of zero corresponds-given a normal distribution-to the representative mean of admission and discharge data of all patients at the clinical trial center. A z-value of 1, corresponds to a deviation from the mean by one standard deviation. Z-differences with no significant changes are in a range of 0.00 ± 0.20. Changes from admission to discharge are illustrated by effect sizes. In addition, the number of patients (relative frequency in %) is stated, which could improve clinically (categorical representation: better, equal, and worse). The threshold used is an average z-difference (~SMD) >0.20 (MED 1–3, ORT 1–3) or >0.33 (unspecific Health Index, Specific Ortho Index, and overall medical quality outcome). Alternatively, the average (percentile) change compared to the time of admission is calculated and, if necessary, treated according to the indication.

Statistical data processing was performed using IBM® SPSS® Statistics (version 22). In addition to descriptive methods, statistical analysis included parametric methods such as multifactorial variance analyses for repeated measures [(M)AN(C)OVA; between-effects: gender (2), covariate: age, within-effect: rehabilitation course (2)], regression analysis and Pearson correlations. Individual missing values were not replaced for statistical analysis. The specification of p-values was omitted, instead effect sizes were used [partial Eta^2 and standardized mean differences (Cohen's d or z-values/-differences, SMD)]. The representation of the partial Eta^2 (η^2) was chosen because even the very small numerical differences became statistically significant even if they were not relevant in terms of content and clinical relevance. A η^2 between 0.01 and 0.06 corresponds to a small effect. Occurrences of 0.06–0.14 correspond to a middle effect and values >0.14 to a large effect [49]. The application of multivariate variance analyses (MANOVA) and a factor-analytical reduction of the basic clinical data to individual factors or a total value (MQO) follow substantive, statistical considerations for better clarity.

3. Results

The effect of the rehabilitation stay and the change between the initial state and the discharge state differ between the individual success factors for medical rehabilitation (see **Tables 4**, **6** and **7**). Specific and unspecific outcomes show a comparable change in sensitivity ($\eta^2_{unspecific} = 0.522$ [UH_i] vs. $\eta^2_{specific} = 0.540$ [SO_i]). The relationship between specific and unspecific outcome characteristics (changes) is small ($r < 0.20$, see **Figure 1** and **Table 5**), which is reflected in a multivariate analysis of temporal changes in the variance ($\eta^2_{unifactorial}$ = 0.654 [MQO_i]).

The nonspecific overall score-the “Health Index (UH_{Index})”-shows that 72.5% of patients benefit directly from the rehabilitation stay. About 21.8% of the patients remain unchanged and 5.8% worsen between the beginning and the end of the rehabilitation (see **Table 4**). The detailed analysis of average improvement in general health features by 13.58 percentile points shows that anatomical features, such as body mass index and abdominal circumference, remain unchanged over the 3 weeks in the majority (86.4%). By contrast, cardiovascular features such as blood pressure and resting heart rate are directly influenced by inpatient rehabilitation, with an average improvement of 11.5 percentile points. The most pronounced effects of inpatient rehabilitation can be seen in the symptoms of complaints, where almost every rehabilitation (84.9%) reported a significant improvement. A similarly positive change can be seen in the ADL score (+17.6 percentile points), motor function (+22.2 percentile points) and physical performance, where 2/3 (67.5%) of patients can improve markedly.

[%]	better	equal	worse	Ø-improvement*
MED1: Anatomy (BMI, AC)	11,2	86,4	2,4	*MED1: +1,33*
MED2: Physiology (BP, RHR)	56,5	15,7	27,8	*MED2: +11,50*
MED3: Discomfort (VAS, SHS)	84,9	9,9	5,2	*MED3: +27,89*

BMI… Body Mass Index, AC … Abdominal Circumference, BP… Blood Pressure, RHR… Resting Heart Rate, VAS… Visual Analog Skale (pain), SHS… Subjective Health Status (EQ-VAS); Threshold for classification: MED1-3: 0,20 (z-difference);

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[relative frequency in %]	**better**	**equal**	**worse**	**Ø-improvement***
Unspecific Health Index	72,5	21,8	5,8	*UH_{Index}: +13,58*
Specific Ortho Index	77,0	19,0	4,0	*SO_{Index}: +17,70*
Overall Medical Quality Outcome	**81,3**	**16,4**	**2,3**	***MQO_{Index}: +15,62***

**. Average improvement (percentiles) from admission to discharge;*
Threshold for classification Unspecific Health, Specific Ortho & overall Medical Quality Outcome Indices ~0,33 SMD;

[%]	better	equal	worse	Ø-improvement*
ORT1: ADL (EQ5D)	58,6	33,1	8,3	*ORT1: +17,57*
ORT2: Function (RM, WOMAC or CM)	76,3	18,0	5,6	*ORT2: +22,17*
ORT3: Physical Ability (WT)	67,5	30,7	1,8	*ORT3: +12,96*

ADL… Activities of Daily Living, RM… Roland Morris, CM… Constant Murley, WT… Walking Tests;
Threshold for classification: ORT1-3: 0,20 (z-difference);

Table 4. Overview of medical quality outcomes.

Almost all considered medical factors (MED, ORT) provide a comparable contribution to the overall success (MQO, all $r \geq 0.40$, except for MED1: $r = 0.11$). The correlation between Unspecific Health Index and Specific Ortho Index is relatively low ($r = 0.19$; see **Figure 1** and **Table 5**). Therefore, immediate changes in unspecific health scores are not directly associated with improvements in (indication-) specific functional characteristics. One exception is the (subjective) complaints (MED 3), which are related to specific outcome changes ($r = .34$).

However, the extent of improvement in medical outcome and the effect size are similar in all areas (see **Tables 4**, **6** and **7** and **Figure 1**). Just the anatomy factor (MED 1) changed only slightly during rehabilitation ($\eta^2_{MED1} = 0.072$; **Tables 6** and **7**). The individual parameters for all patients are presented in **Tables 6** and **7** below.

3.1. Output values and descriptive data for individual measurements

The starting point (initial) values of rehabilitation clearly show the deficits of the affected patients (see **Tables 6** and **7**). The average BMI is 28.9 ± 5.4 units (37.0% of patients have a BMI > 30) and 77.3% of patients have "high-normal" or "hypertonic" blood pressure. The perceived pain (VAS; 0–10) of patients is 3.8 ± 2.1 and the subjective health status (EQ-VAS; 0–100) is estimated to be 63.7 ± 16.6% on average.

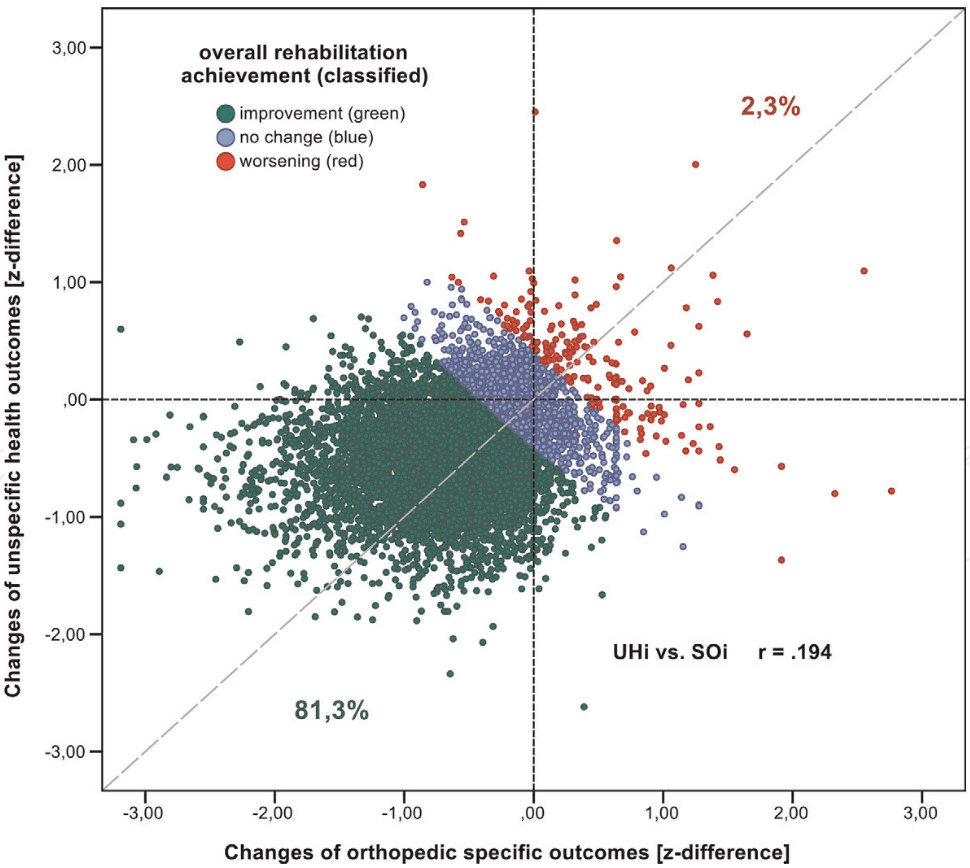

Figure 1. A value of zero (± 0.20 [z]) stands for no significant changes from admission to discharge (blue dots). The mean for UHi is −0.45 ± 0.43 and for SOi −0.59 ± 0.55. The overall MQOi (mean of UHi & SOi) is −0.52 ± 0.38 (centroid).

Correlation of changes in medical factors [Pearson]		MED 1 (Anatomy)	MED 2 (Physiology)	MED 3 (Discomfort)	UH_i (Unspecific health ind.)	Overall MQO (medical quality outcome)
ORT 1 (ADL)	r	0.000	−0.007	0.285	0.162	**0.671**
	p	0.982	0.496	0.000	0.000	0.000
ORT 2 (Function)	r	0.012	−0.006	0.314	0.183	**0.638**
	p	0.288	0.620	0.000	0.000	0.000
ORT 3 (Physical ability)	r	−0.020	−0.011	0.072	0.033	**0.399**
	p	0.113	0.406	0.000	0.010	0.000
SO_i (Specific Ortho Index)	r	−0.002	−0.009	0.340	0.194	**0.833**
	p	0.878	0.385	0.000	0.000	0.000
Overall MQO (medical quality outcome)	r	**0.107**	**0.444**	**0.579**	**0.704**	**1**
	p	0.000	0.000	0.000	0.000	

Bold values show the correlation of each health parameter with the overall medical quality outcome.

Table 5. Correlations between changes in MQO factors.

MQO indicators & factors	Initial values (beginning of rehabilitation; prae)		Change from admission (prae) to discharge (post)				
Measure	**Mean ± standard deviation (SD)**		**Mean diff. (post-prae) ±SD**		**(*z*) Normalized difference ± SD**		**part. Eta²**
BMI [kg/m²]	28.89	5.38	−0.15	1.45	−0.03	0.27	0.011
Abdominal circumference [cm]	100.24	13.71	−0.99	2.78	−0.07	0.20	0.114
MED 1: Anatomy [z]	**0.10**	**0.97**	**−0.05**	**0.18**	**−0.05**	**0.18**	**0.072**
RRsys [mmHG] (blood pressure systolic)	130.74	11.30	−4.78	13.00	−0.37	1.02	0.119
RRdia [mmHG] (blood pressure diastolic)	76.87	7.45	−2.28	9.44	−0.29	1.19	0.055
heart rate [bpm]	78.74	11.67	−1.41	12.13	−0.12	1.01	0.014
MED 2: Physiology [z]	**0.14**	**0.89**	**−0.37**	**1.01**	**−0.37**	**1.01**	**0.120**
VAS [cm; 0–10] (pain)	3.75	2.14	−1.68	1.69	−0.70	0.70	0.501
self-rated health [%; 0–100] (EQ-VAS)	63.70	16.60	13.79	14.84	−0.80	0.86	0.465
MED 3: Discomfort [z]	**0.45**	**0.92**	**−0.91**	**0.75**	**−0.91**	**0.75**	**0.598**
UH: unspecific health Index [z] MED1, MED2, MED3	**0.23**	**0.59**	**−0.45**	**0.43**	**−0.45**	**0.43**	**0.522**

Bold values show summarized factors of outcome measures from unspecific general health parameters (see **Table 2**).

Table 6. Starting point values and changes in individually measures quantities.

MQO indicators & factors	Initial values (beginning of rehabilitation; prae)		Change from admission (prae) to discharge (post)				
Measure	**Mean ± standard deviation (SD)**		**Mean diff. (post - prae) ± SD**		**(z) Normalized difference ± SD**		**part. Eta²**
ORT 1: ADL [0-100 & z] (activities of daily living; EQ5D)	**68.36**	**24.36**	**9.22**	**13.20**	**−0.59**	**0.84**	**0.361**
Roland-Morris [0–24]	8.42	5.26	−3.16	3.92	−0.59	0.73	0.394
WOMAC [Sum; 0–240]	73.70	42.17	−32.54	32.26	−0.77	0.77	0.504
Constant-Murley [Sum; 0–100]	41.09	17.19	17.98	11.53	−0.91	0.58	0.709
ORT 2: Function [z]	**0.36**	**0.97**	**−0.73**	**0.73**	**−0.73**	**0.73**	**0.475**
Time up & go [sec]	11.04	6.49	−2.62	3.30	−0.46	0.58	0.393
10m [sec]	9.55	5.23	−1.95	2.88	−0.43	0.63	0.327
ORT 3: Physical ability [z]	**0.22**	**1.11**	**−0.44**	**0.55**	**−0.44**	**0.55**	**0.403**
SO: specific ortho index [z] ORT1, ORT2 & ORT3	**0.31**	**0.83**	**−0.59**	**0.55**	**−0.59**	**0.55**	**0.583**

Bold values show summarized factors of outcome measures from disease-specific health parameters (see **Table 2**).

Table 7. Initial values and changes in individual measurements.

Unspecific and indication-specific outcome data (see **Tables 6** and **7**) show clear success during the rehabilitation stay, with complaints (MED 3, η^2 = 0.598) and motor function (ORT 2, η^2 = 0.478) improving markedly within the 3 weeks.

Based on the subsample survey of knee and hip TEP patients, it can be seen that changes occur in the nonspecific factors independent of the time of rehabilitation (interaction: time x post-op week: η^2 = 0.001). This result is in contrast to (disease-specific) outcome characteristics (SOi) where the time of onset (post-op week) plays a more important role (interaction: η^2 = 0.061; see **Table 9** (cf. [26]).

3.2. Comparison of outcomes based on ICD-classification

If one considers the initial medical evaluation values and changes there of as a result of the inpatient rehabilitation stay, we need to evaluate also the initial severity and admission diagnosis. The admission diagnosis was evaluated based on the standardized ICD-10 classification ("ICD") (see **Tables 8** and **9**). This classification shows that knee patients have worse MED 1 (Anatomy) values at the beginning of rehabilitation (0.36 ± 0.96). In back pain patients, especially negative MED 3 initial medical evaluation values (Discomfort) are prominent (MED 3: η^2 = 0.068). The symptom-specific characteristics (ORT, SO_i) and their differences in initial values were somewhat less pronounced (SO_i: η^2 = 0.010 vs. UH_i: η^2 = 0.017; see **Table 9**).

Overall adding up the MQO factors, the initial medical evaluation values are comparable between the ICD diagnostic groups (η^2_{MQOi} = 0.004), but in individual cases, they certainly play an important role ($\eta^2_{multivariat}$ = 0.080, see **Table 9**).

3.3. Influencing factors of age, gender and initial values

Depending on further grouping characteristics (between factors), it is shown that gender ($\eta^2_{multivariat}$ = 0.076) and age ($\eta^2_{multivariat}$ = 0.067) contribute a significant amount to initial values, which is lower within unspecific than in specific parameters (see **Table 9**; (cf. [26]). Additionally, medical initial values are influenced by the factor injuries (*S*) vs. chronic conditions (*M*; $\eta^2_{multivariat}$ = 0.058), as well as the symptom presentation "ICD" ($\eta^2_{multivariat}$ = 0.080).

Potential success through rehabilitation with unspecific outcome indicators (changes of condition pre and post, see also **Table 4**) can be observed within all grouping characteristics of a similar magnitude (interaction time x between factor: $\eta^2_{UHi} < 0.003$ see **Table 9**). In contrast, age, ICD, postOP and initial value of MQO play a role for alterations in specific outcome indicators (Age: η^2_{OHi} = 0.039, ICD: η^2_{OHi} = 0.040, postOP: η^2_{OHi} = 0.061 and initial MQO value: η^2_{OHi} = 0.143). All these factors influence the specific outcome significantly. Older patients (>61 years of age), patients with knee and hip issues, patients who enter phase 2 earlier after surgery (<6 weeks) and particularly patients with worse medical initial values show a more advantageous rehabilitation outcome for symptom-specific indicators (not shown).

MQO indicators & factors		Initial values (beginning of rehabilitation; prae)		Change from admission (prae) to discharge (post)		
Classification according to ICD-10 (cf. Table 3)		**Mean* ± standard deviation (SD)**		**Mean diff.** (post - prae) ± SD**		**part. Eta^2**
MED 1: anatomy	hip	0.15	0.94	−0.05	0.17	0.069
	knee	0.36	0.96	−0.06	0.18	0.086
	back (spine)	0.06	0.97	−0.05	0.19	0.058
	total	**0.18**	**0.97**	**−0.05**	**0.18**	**0.068**
MED 2: physiology	hip	0.19	0.90	−0.38	1.02	0.120
	knee	0.18	0.84	−0.34	1.00	0.107
	back (spine)	0.13	0.93	−0.40	1.03	0.129
	total	**0.16**	**0.89**	**−0.37**	**1.01**	**0.116**
MED 3: discomfort	hip	0.07	0.90	−0.83	0.68	0.600
	knee	0.38	0.86	−0.91	0.73	0.610
	back (spine)	0.65	0.92	−0.99	0.79	0.610
	total	**0.43**	**0.93**	**−0.92**	**0.74**	**0.596**
UHi: unspecific health Idx	hip	0.14	0.57	−0.42	0.40	0.517
	knee	0.31	0.57	−0.44	0.42	0.516
	back (spine)	0.28	0.61	−0.48	0.44	0.538
	total	**0.26**	**0.59**	**−0.45**	**0.43**	**0.515**
ORT 1: ADL	hip	0.37	1.09	−0.84	0.95	0.437
	knee	0.34	0.96	−0.69	0.86	0.390
	back (spine)	0.23	0.97	−0.52	0.80	0.295
	total	**0.30**	**1.00**	**−0.66**	**0.87**	**0.378**
ORT 2: function	hip	0.25	0.99	−0.78	0.77	0.507
	knee	0.37	0.96	−0.78	0.76	0.507
	back (spine)	0.27	0.97	−0.61	0.73	0.411
	total	**0.30**	**0.97**	**−0.71**	**0.76**	**0.473**

MQO indicators & factors		Initial values (beginning of rehabilitation; prae)		Change from admission (prae) to discharge (post)		
Classification according to ICD-10 (cf. Table 3)		**Mean* ± standard deviation (SD)**		**Mean diff.** (post - prae) ± SD**		**part. Eta^2**
ORT 3: physical ability	hip	0.37	0.93	−0.53	0.53	0.505
	knee	0.24	0.84	−0.47	0.47	0.498
	back (spine)	-0.07	0.98	−0.31	0.43	0.339
	total	**0.15**	**0.94**	**−0.42**	**0.48**	**0.456**
SOi: specific ortho Idx	hip	0.32	0.81	−0.72	0.55	0.633
	knee	0.32	0.73	−0.64	0.49	0.630
	back (spine)	0.16	0.78	−0.48	0.46	0.513
	total	**0.26**	**0.77**	**−0.60**	**0.51**	**0.597**
MQOi: overall idx	hip	0.23	0.56	−0.57	0.37	0.703
	knee	0.31	0.54	−0.54	0.36	0.697
	back (spine)	0.22	0.58	−0.48	0.36	0.641
	total	**0.25**	**0.56**	**−0.52**	**0.36**	**0.677**

*Positive (z-) values show a bad initial state at the beginning of rehabilitation.
**Negative (z-normalized) differences show an improvement from admission to discharge.
Bold values show overall means of summarized medical quality factors for the three most common orthopedic diagnoses.

Table 8. Symptom-specific (ICD) MQO.

Factors (main effects)	**Unifactorial part. Eta^2 for initial values (prae)***					**Unifactorial part. Eta^2 for changes (prae-post; interaction)****					
Between factors:	Sex	Age	Type	ICD***	Post-OP	Sex	Age	Type	ICD	Post-OP	Initial value$_{MQO}$
MQO variables	f/m	4-stage	M/S	**h/k/b**	5-stage	f/m	4-stage	M/S	h/k/b	5-stage	3-stage
MED 1: anatomy	0.018	0.023	0.024	**0.013**	0.001	0.004	0.005	0.000	0.001	0.001	0.006
MED 2: physiology	0.018	0.003	0.001	**0.000**	0.003	0.002	0.001	0.000	0.000	0.001	0.023
MED 3: discomfort	0.013	0.007	0.001	**0.068**	0.016	0.005	0.002	0.000	0.007	0.002	0.042
Unspecif. health$_{Idx}$	**0.007**	**0.011**	**0.007**	**0.017**	**0.007**	**0.000**	**0.001**	**0.001**	**0.003**	**0.001**	**0.061**
ORT 1: ADL	0.028	0.041	0.011	**0.003**	0.012	0.006	0.021	0.000	0.022	0.033	0.055
ORT 2: function	0.012	0.029	0.003	**0.002**	0.005	0.005	0.009	0.000	0.012	0.021	0.085
ORT 3: physical ability	0.032	0.161	0.027	**0.042**	0.020	0.009	0.041	0.005	0.040	0.048	0.094
Specific ortho$_{Idx}$	**0.036**	**0.103**	**0.018**	**0.010**	**0.015**	**0.013**	**0.039**	**0.001**	**0.040**	**0.061**	**0.143**
MQO$_i$: overall$_{idx}$	**0.009**	**0.061**	**0.003**	**0.004**	**0.004**	**0.006**	**0.021**	**0.000**	**0.011**	**0.033**	**0.168**
Multivariate (Pillai's trace)	**0.076**	**0.067**	**0.058**	**0.080**	**0.016**	**0.022**	**0.020**	**0.006**	**0.040**	**0.020**	**0.103**

Between factor: sex (female, male), age (quantile; ≤ 52, 53–61, 62–72, 73+), type (disease [M], injury [S]), ICD (hip, knee, back/spine), post-OP (period between surgery and rehabilitation; ≤ 6 weeks, 43–70 days, 71–105 days, 106–366 days, >1 year), initial value MQO (tertile); A part. Eta2 ($\eta 2$) between 0.01–0.06 corresponds to a small effect, occurrences of 0.06–0.14 a middle effect and values >0.14 a large effect.

*Initial state at the beginning of rehabilitation.

**Differences (improvements) from admission to discharge (corresponds to the interaction: time x factor).

***C.f. **Table 8**.

Bold values show the influence (effect size) of the approval diagnosis on baseline values and the impact of other moderating variables on summarized unspecific and specific health factors.

Table 9. MQO and potential influence factors.

4. Discussion

In times of dwindling resources, evidence-based justifications of medical measure effectiveness are gaining ever more practical and healthcare economic importance. New possibilities of medical treatment measures and constantly changing framework conditions are a challenge for quality assurance management, which uses structural, process and outcome characteristics to evaluate the degree to which predefined goals have been achieved. Potential environmental influences or a change of framework conditions can also be evaluated with regard to the MQO. The recorded routine data are used both as an evaluation criterion and as comparison data of the expected MQO or output values.

Current treatment paths emphasize a stratified approach, active therapies and educational measures, whereby evidence of effectiveness and clinical practice still clearly diverge [28, 50, 51].

Based on presented clinical observations through routine operating procedures of a multidisciplinary inpatient musculoskeletal system rehabilitation, evaluation can be performed. The evaluation takes into account facility and patient comparisons and is based on standardized assessments of different treatment options as well as factors of outcome quality. Existing performance profiles have a certain amount of latitude to focus on treatment or to apply promising therapeutic options. Such differentiated treatment pathways are necessary for efficient and successful treatment so that individual patients or specific patient groups can be addressed.

A physician/therapist or facility can use the results presented to make an evidence-based decision relatively quickly on whether the treatment process is proceeding to their satisfaction. Orthopedic patients receive a realistic assessment of what and how much they will improve their physical abilities through the 3-week inpatient medical treatment.

The selection of outcome parameters follows evidence-based and economic considerations that should guarantee a comparable standard of quality medical treatment. Indication-specific characteristics (ORT, SO_i) are at the center of the rehabilitative treatment, to restore the ability to function and work or to reintegrate into the social and professional environment. Another focus is on nonspecific health features such as individuals that are overweight, have high blood pressure or are physically inactive. These characteristics are associated with poorer health, cardiovascular disease and metabolic disorders. They are among the most important variable risk factors for chronic diseases and premature death [52].

An important task in inpatient rehabilitation is, in addition to the individual symptomatic treatment of a patient, to sustainably reduce these risk factors. Quality of life and functioning are characterized by positive lifestyle modifications, for example, an increase in physical activity. A reduction in the recorded basic clinical parameters such as BMI, abdominal circumference, blood pressure, heart rate and pain [53–56] is therefore also highly relevant in the inpatient rehabilitation of degenerative and inflammatory disorders of the musculoskeletal system [57, 58]. A mathematical comparison with "healthy" patient reference data underlines the importance of the MQO factors presented in this work, which deviate in the order of about one standard deviation of healthy individuals.

In order to work meaningfully and deductively, it is helpful to reduce the abundance of partially redundant information to a manageable, uniform level. An additive summary of independent medical areas (factors) to a key figure (UH_i or SO_i and overall MQO) is to be discussed in terms of content and statistics. These key figures give a simple and quick overview of the "unspecific" effectiveness of the rehabilitative stay for certain healthcare teams or treatment programs.

4.1. Nonspecific quality of outcomes

When assessing the effectiveness of inpatient rehabilitation based on the nonspecific health outcome characteristics, it is not so important to use grouping characteristics such as symptoms. Grouping based on gender and age is here too of minor importance. Comparing the values at discharge with the initial medical evaluation data shows that 72.5% of patients benefit directly from inpatient rehabilitation (see **Table 4**). Significant interactions with grouping features are present but can be classified as "small" compared to the main effects ($\eta^2 < 0.003$; see **Table 9**). The observed strong rehabilitation effect is similar for all subgroups ($\eta^2 > 0.500$; see **Tables 6** and **8**). This unspecific success is probably attributable to all inpatient rehabilitation stays and to the preventive effect of activity or movement in the rehabilitation setting.

The change in the nonspecific MQO is independent of the time of rehabilitation, the post-OP week ($\eta^2_{UHi} < 0.001$; see **Table 9**). In an untreated "real" control group without rehabilitation, therefore, no positive change in the constitutional state of health is to be expected.

In contrast, the importance of early inpatient rehabilitation as early as possible is revealed in disease-specific outcome characteristics such as function or physical ability ($\eta^2_{OHi} = 0.061$). This underlines the importance of a multidimensional view of specific and nonspecific outcome quality, describing two independent (active) components of rehabilitation (see **Figure 1** and **Table 5**).

4.2. Specific quality of outcomes

The most pronounced effects of inpatient rehabilitation are seen in the complaint (MED 3) and indication-specific characteristics (ORT 2, ORT 3 and SO_i). More than 2/3 of patients experience significant improvement of symptoms and specific characteristics (see **Table 4**). About 77.0% of patients show indication-specific improvement of outcomes in inpatient rehabilitation. However, 19.0% did not show significant changes and 4.0% showed worsening from rehabilitation beginning to rehabilitation end. Therefore, it is important to remember that not all patients can directly benefit from treatment. In sum, (overall MQO) improvement is achieved, in the vast majority (81.3%, SMD = 0.52 ± 0.38; see **Figure 1**). Improvement of unspecific and indication-specific outcome parameters is achieved in a comparable magnitude.

Unlike nonspecific health scores, moderating factors play a more important role in the specific outcome quality. In particular, patients who enter Phase II earlier (<6 weeks) after surgery and patients with worse initial medical evaluation show better rehabilitation success in symptom-specific characteristics (see **Table 9**).

4.3. The applicability of our results in rehabilitative clinical practice

Despite large international differences in healthcare teams and treatment measures in rehabilitation, the observed effect sizes can support individual evaluation but cannot replace it. In addition to case by case evaluation, it is important to consider the medical focus, the rehabilitative practice and performance profiles, as documented outcomes come about through different treatment programs and the associated different use of healthcare resources.

Absolute values and individual profiles of the MQO should always be evaluated according to the given setting and at the doctor's discretion. Single measurements are subject to a variety of moderating influences and measurement errors. The presented continuous measures of MQO have advantages in terms of their (scale) properties and sensitivity to frequently applied categorical criteria.

When using the presented clinical reference values of the MQO for orthopedic rehabilitation (WHO phase II) in Austria, apart from the reference sample, the monocentric character of the work has to be considered. The need for adjusting for different facility comparisons cannot be definitively answered. Different individual starting values must always be taken into account, as worse outcome parameters at the beginning of rehabilitation are accompanied by a greater potential for improvement (e.g., $r_{MQO} = -0.461$). Due to the prescribed performance profiles and the centrally controlled assignment modalities by the insurers, however, it can be assumed that the initial values presented and especially the changes in the MQO are representative of the inpatient rehabilitation of the musculoskeletal system in Austria.

The presented results and experiences of the clinical trial center suggest that the expected rehabilitation effects in the MQO factors are universal. Risk adjustment or indication- and group-specific modeling does not seem necessary. A closer characterization of nonresponders and types is still pending.

4.4. Limitation

The practical significance of the MQO outcomes or relationships with external criteria (endpoints), such as the incapacity for work, remains to be tested. Especially the global evaluation between MQO and sociomedical relevant external criteria is a potential further route for development. It is to be clarified which of the observed changes in MQO have significance for the sustainability of rehabilitative measures and to what extent optimized treatment pathways can influence them. Improvements in one outcome may well be accompanied by deterioration in other outcomes. Therefore, multidimensional approaches to the quality of results are always the methods of choice.

5. Conclusions

In addition to the usual "primary patient-oriented" assessment of quality of outcomes, the subjective assessment and satisfaction through self-reporting of patients as well as quality registers on surgical frequencies, length of stay and complications, these factors present a valuable addition to the medical outcome quality evaluation. These can be essential for decision-making or can contribute to the design processes and further developments of quality assurance in rehabilitation facilities.

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Conflict of interest

The authors declare no conflict of interest.

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Dynamics of Vagal Activity Due to Surgery and Subsequent Rehabilitation

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Background: Vagal activity is critical for maintaining key body functions, including the stability of inflammatory control. Its weakening, such as in the aftermatch of a surgery, leaves the body vulnerable to diverse inflammatory conditions, including sepsis.

Methods: Vagal activity can be measured by the cardiorespiratory interaction known as respiratory sinus arrhythmia or high-frequency heart-rate variability (HRV). We examined the vagal dynamics before, during and after an orthopedic surgery. 39 patients had their HRV measured around the period of operation and during subsequent rehabilitation. Measurements were done during 24 h circadian cycles on ten specific days. For each patient, the circadian vagal activity was calculated from HRV data.

Results: Our results confirm the deteriorating effect of surgery on vagal activity. Patients with stronger pre-operative vagal activity suffer greater vagal withdrawal during the peri-operative phase, but benefit from stronger improvements during post-operative period, especially during the night. Rehabilitation seems not only to efficiently restore the vagal activity to pre-operative level, but in some cases to actually improve it.

Discussion: Our findings indicate that orthopedic rehabilitation has the potential to strengthen the vagal activity and hence boost inflammatory control. We conclude that providing a patient with a vagal reinforcement procedure *prior* to the surgery ("pre-habilitation") might be a beneficial strategy against post-operative complications. The study also shows the clinical usefulness of quantifying the cardiorespiratory interactions.

Keywords: circadian rythm, surgery, vagal tone, inflammatory control, rehabilitation

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INTRODUCTION

Vagus nerve is the longest nerve of the autonomic nervous system (ANS) and the key component of parasympathetic nervous system. Its baseline activity, often refered to as *vagal activity*, is crucial for maintaining several body functions at rest, including heart, lungs, and digestion. Vagal activity is stronger during sleep, stabilizing the body's circadian rhythms, which are key for good general health (Mundigler et al., 2002; Moser et al., 2006a; Kastner et al., 2010; Rocha et al., 2011; Scheiermann et al., 2013; Curtis et al., 2014; Papaioannou et al., 2014; Alamili, 2015; Madrid-Navarro et al., 2015; Wright et al., 2015).

Vagal activity is also the critical factor behind the functionality of the *inflammatory reflex*, mechanism responsible for resolving the inflammation once its purpose has been served

(Tracey, 2002, 2007; Moser et al., 2008; Rosas-Ballina and Tracey, 2009; Leslie, 2014; Mayer, 2015). Actually, the vagal inflammatory reflex involves 80% vagal afferents and 20% efferents, which means that four times more information is collected by the brain than transmitted to the periphery: macrophages in the inflamed tissue produce inflammation signals such as TNF-alpha and interleukin 1 (Andersson and Tracey, 2012; Olofsson et al., 2012), which attract other monocytes from nearby blood vessels. Vagal afferents carry receptors for these signals and communicate with certain stem brain areas transmitting the information on inflammation location and strength (Andersson and Tracey, 2012). Upon processing this information, vagal efferents respond by release of acetylcholine at the location of the inflamed tissue (Olofsson et al., 2012). Nicotinergic acetylcholine receptors have been identified on the surface of the macrophages, which down-regulate their cytosine production as a response to the cholinergic stimulation (Rosas-Ballina and Tracey, 2009), thereby reducing the attraction of additional inflammatory immune cells. This inflammatory reflex loop prevents over-activity of the immune system enabling the brain to locally control the immune activity. It also represents the "first line" of inflammation control (Olofsson et al., 2012).

In addition to improving the effectiveness and usefulness of the inflammatory reflex, a strong vagal activity protects against several serious or chronic conditions. They include atherosclerosis, ulceral colitis, Hashimoto's disease, type 2 diabetes, cancer (Donchin et al., 1992; Moser et al., 2006a; Das, 2011; Huston and Tracey, 2011; Chow et al., 2014), and sepsis, which is know to be related to weakening of body's natural ability to resolve the inflammation (Tracey, 2002; Nguyen et al., 2006; Nathan and Ding, 2010). The vagus nerve can be electrically and pharmacologically stimulated, while its overall activity can be improved via acupuncture, nutritional therapies, and physical exercise (Huang et al., 2005; Moser et al., 2017).

Measuring vagal activity can be reliably done by analyzing the heart rate variability (HRV). In fact, HRV is created by the interaction between ANS and the sinus node of the heart (Moser et al., 1995). Its main component, originating in vagal activity, is respiratory modulation of the heart frequency. Through a gating process that takes place in the brainstem, vagal activity is responsible for speeding up the heart when we breath in, and slowing it down when we breath out (Langhorst et al., 1983). The amplitude of this respiratory sinus arrhythmia is proportional to the vagal activity. This cardiorespiratory interaction mediated by the vagus nerve is faster (approximately 0.25 Hz) than other influences of the ANS (0.1 Hz or slower). Actually, postsynaptic vagal activity is mediated by acetylcholine, which is rapidly degraded in the synaptic gap by its esterase, an enzyme that warrants fast decay of neurotransmitters after release. This makes the parasympathetic synapses much faster than the sympathetic ones, which use norepinephrine postsynaptically (Moser et al., 1998). Norepinephrine is eliminated mainly by presynaptic reuptake, which results in transmitters remaining longer in the synaptic gap. In short, the intensity of this cardiorespiratory interaction can be used as a reliable measure of vagal activity (Moser et al., 1994).

Surgery is a situation where it is paramount to preserve the strong vagal activity. There is aboundant evidence that surgical procedures weaken the vagal activity (Donchin et al., 1992; Munford and Tracey, 2002; Williamson et al., 2010), while surgery is a notorious trigger of sepsis. With this in mind we performed a clinical study aimed at testing the effects of surgery on patient's vagal activity. Our study relies on a longitudinal measurement and comparison of circadian dynamics (24 h recordings) of vagal activity in patients before, during and after a surgical procedure. This includes measurements during and after rehabilitation, for up to 1 year after the surgery. Vagal activity is computed from HRV data as described in Moser et al. (1994), Moser et al. (1995), Lehofer et al. (1999).[1] We report our results in what follows.

MATERIALS AND METHODS

Patients and Ethics

Thirty-nine patients (23 female of age 32–83 and 16 male of age 32–81) were recruited for our study. They were hospitalized at the Orthopedic Rehabilitation Center at Humanomed Center in Althofen, Austria for total endoprosthetic orthopedic surgery (replacement of hip or knee joints). Inclusion criteria were age 30–90 and completion of 3 week rehabilitation within 3 months after the surgery. Exclusion criteria were usage of pacemaker and clinically identified complications (thrombosis, pulmonary embolism, or wound healing disorders). Patients were informed about the nature and the purpose of the study, signed the informed consent and participated voluntarily. After the study, personal results were given to all patients with adequate expert explanation. The study was authorized by the Ethical Committee of the Carinthian Government, authorization number A 02/05, 01 February, 2005. Methods were chosen in accordance with the relevant guidelines and regulations.

Measurement Protocol

In order to investigate the behavior of vagal activity in relation to the surgery and the subsequent recovery, we divided the operation-rehabilitation process into the following four phases: immediately before the surgery (*pre-operative phase*), immediately after the surgery (*peri-operative phase*), *rehabilitation,* and long-term recovery (*post-operative phases*). On ten specific days each patient had his/her vagal activity measured over the entire day, i.e., the 24 h circadian cycle. These are referred to as "measurement days" and denoted as T1,T2,. . .T10. They are "time periods" chosen to best reflect each phase of the operation-rehabilitation process as follows.

- *Immediately before the surgery* ("*pre-operative*"; measurement days T1 and T2). Patients were measured on 2 days, sometime between 8 and 2 days prior to the surgery.
- *Immediately after the surgery* ("*peri-operative*"; measurement day T3). Patients were measured on 1 day sometime between 2nd and 4th day after the surgery, depending on their availability due to their medical state.
- *Rehabilitation* ("*post-operative*"; measurement days T4, T5, and T6). Patients were measured on 2nd, 9th, and 16th day

[1] Actually, HRV is long known as a good marker for risk stratification, early prognosis and prediction of post-operative complications.

'pre-operative'		OP	'peri-operative'	'post-operative' (Rehabilitation)			'long-term recovery'			
T1	T2		T3	T4	T5	T6	T7	T8	T9	T10
between 8 and 2 days prior to the surgery		surgery	between 2nd and 4th day after the surgery	26.6 +/- 11.3 days after the surgery	2nd (T4), 9th (T5) and 16th (T6) day of the inpatient rehabilitation		6th (T7), 12th (T8), 26th (T9) and 52nd (T10) week after the end of the rehabilitation			

FIGURE 1 | Shematic representation of the division of operation-rehabilitation process into phases and measurement days for the purposes of our study.

of the inpatient rehabilitation process (rehabilitation started 26.6 ± 11.3 days after the surgery).

- *Long-term recovery* (measurement days T7, T8, T9, and T10). Patients were measured at the beginning of 6th, 12th, 26th, and 52nd week after the end of the rehabilitation.

For better orientation we show in **Figure 1** the schematic representation of this division.

Since previous studies found a strong cure-treatment effects to peak after 6 weeks (Moser et al., 1998; Lehofer et al., 1999), we used this time period to perform the first post-rehabilitation measurements. After this, we used approximate doubles of 6-week-intervals until the end after 1 year, which is a reasonable (almost) exponential frame for observing long-term effects. These measurements are taken on as equidistant time-points as patients compliance allowed.

HRV Measurements

On each measurement day we made precise circadian measurements of heart-rate variability (HRV) for each patient. That is to say, each patient had his/her instantaneous heart rate recorded continuously for 24 h, using a mobile 8000 Hz Holter-ECG with 16 bit A/D converter (ChronoCord, manufacturer: Joysys, Austria), developed from space medical research (Gallasch et al., 1997). The instrument was attached to a patient in a way not to interfere with his/her regular daily activities. Vagal activity was computed from these time series of around 100,000 heartbeats per patient/day as described below, and then averaged over 5 min intervals distributed evenly over 24 h. After this averaging, one circadian time series consisted of 1440 values, i.e., 1 value per each minute of the measurement day. Thus, on each measurement day we obtained for each patient a circadian time series with 1440 HRV values. We defined the *circadian time* from noon on a measurement day to noon on the following day. Our study lasted for over an entire year (408 ± 34,3 days) for each patient (not all patients participated simultaneously). 16 of them completed all the measurements (age 32–81, 11 female). For these 16 patients, some data points were still missing (13.75%). We report the data here only from these 16 patients.

Pre-processing and Computation of the Vagal Activity

Pre-processing steps included filtering and removal of the artifacts, done according to Lehofer et al. (1999). R peaks were detected from the ECG recordings by a digital filter described in Moser et al. (1994), Lehofer et al. (1999) to more than 1 ms accuracy. We then computed the vagal activity time series from the cardiorespiratory arrhythmia by the robust time-domain method named *logRSArr*. The method is described and evaluated in Moser et al. (1994), Lehofer et al. (1999) and its relaton with cardiorespiratory interactions is established in Topçu et al. (2018). In short, we used the formula:

$$\text{Vagal activity} = \log_{10}\left(median_{(5\,\min)}\,|RR_{i+1} - RR_i|\right),$$

where RRs are the consecutive inter-beat (RR) intervals, and the median value is taken over the 5 min interval. This logRSArr method acts as a filter emphasizing high-frequency HRV components, and reflects the vagally mediated respiratory component of HRV better than RMSSD or high frequency HRV (Topçu et al., 2018). Also, the chosen method is more robust than frequency-domain methods and allows a higher time-resolution. Robustness is here important since it prevents the results from disturbances by movement artifacts and ectopic heartbeats. Upon computation, we focused our analysis on these data, which consist of one circadian time series of vagal activity values for each patient on each measurement day.

Statistical Analysis

General linear models (GLM) were used to perform a per protocol analysis via repeated measures ANOVA. Within-subject factor is "time period" [pre-operative (individual means of T1 and T2), peri-operative (T3), rehabilitation (T4, T5, and T6), and long-term recovery (T7, T8, T9, and T10)] for three different "activity periods" of vagal activity within a day (logRSArr during "sleep," "wake," and "24 h mean"). The calculation of the used periods "sleep" and "wake" is based on visual controlled activity protocols of the patients, whereby transitions between wake and sleep, the first and last 30 min of each activity period, were not taken into account. For these statistical analyses, missings (in already aggregated values) in "time period" had to be replaced by individual means of nearby time points in 11 out of 192 cases (5.7%). Later we add pre-operative "vagal-type" as between-subject factor, computed via median split of aggregated 24 h means of logRSArr from T1 and T2 (pre-operative vagal activity) to quantify a hypothesized interaction (time course x vagal-type) for a different development in time course of subjects with a constitutional high vs. low vagal activity.

RESULTS

Overall Circadian Dynamics of Vagal Activity

We first present the overall circadian behavior of vagal activity during operation-rehabilitation process. To this end, we averaged the data over all 16 patients, obtaining one averaged circadian

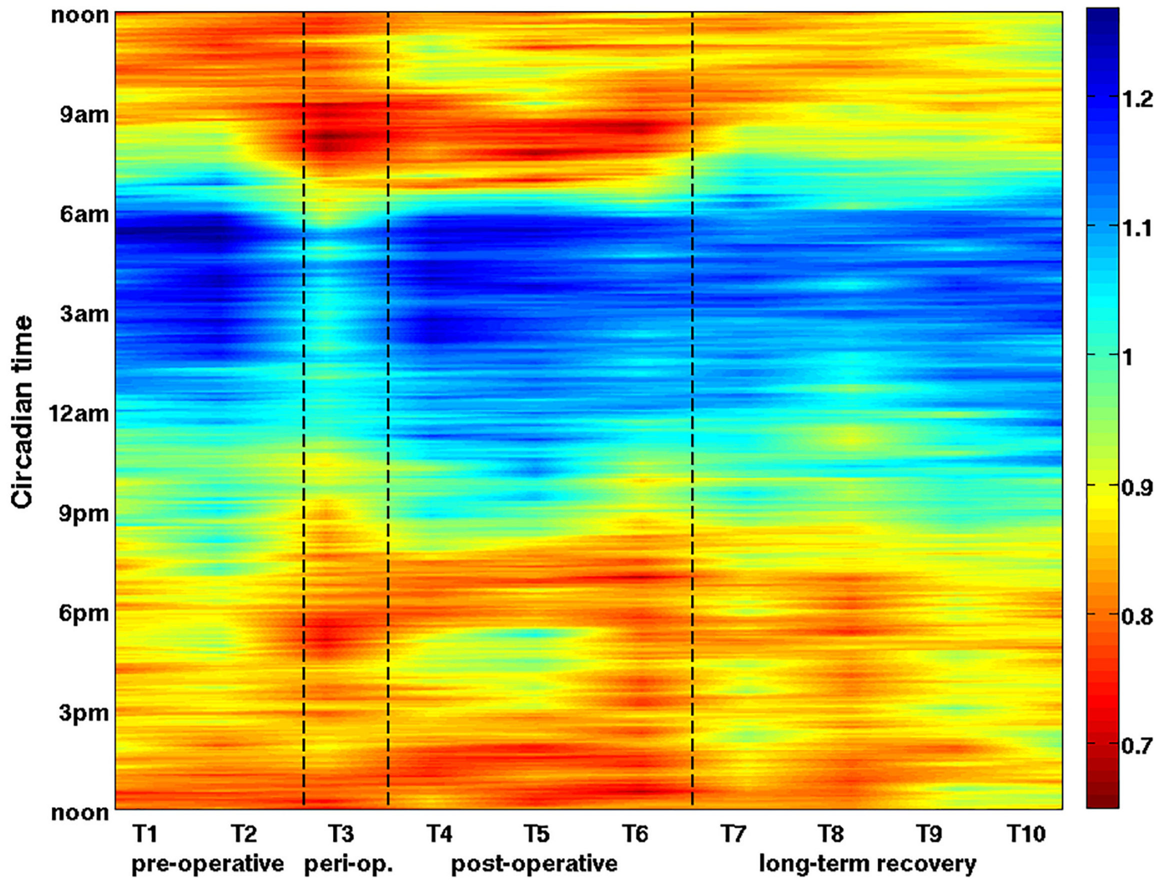

FIGURE 2 | The overall dynamics of the vagal activity during the operation-rehabilitation process. Each color represents the value of the vagal activity averaged over all 16 patients on a given measurement day (horizontal axis, T1–T10) and at a given circadian hour (vertical axis, time runs from bottom to top). Clinical phases are also indicated on the horizontal axis. Each averaged vagal activity value is represented as a color, where red means low and blue means high vagal activity (see color bar). Phases of the operation-rehabilitation process are delimited by the dashed lines. Vagal activity is reduced during peri-operative phase (T3), especially during the night. During the post-operative rehabilitation (T4–T6) original vagal activity values are gradually restored. See also our statistical analysis (**Tables 1**, **2**), which confirms the statistical significance of the vagal activity changes.

TABLE 1 | Statistical significance of vagal activity differences over time.

Repeated measures ANOVA [time (4)]† logRSArr [ms]			Mean	*SD*	*Post hoc* (LSD)	*F*	*P significance*	η_p^2
Time (vagal activity; log RSArr)	Sleep	Pre-operative	1,152	0,175	Pre- vs. Peri-operative (*p* = 0.004**)	4,124	0.025*	0,216
		Peri-operative	1,021	0,172				
		Rehabilitation	1,106	0,233				
		Long-term recovery	1,119	0,271				
		Overall	1,099	0,195	Square time effect	12,739	0.003**	0,459
	Wake	Pre-operative	0,887	0,182		2,189	0.102	0,127
		Peri-operative	0,808	0,183	Peri- vs. Long-term recovery (*p* = 020*)			
		Rehabilitation	0,841	0,244				
		Long-term recovery	0,882	0,203				
		Overall	0,854	0,185	Square time effect	7,475	0.015**	0,333
	Mean-24 h	Pre-operative	0,980	0,155	Pre- vs. Peri-operative (*p* = 0.028*)	3,243	0.046*	0,178
		Peri-operative	0,885	0,170				
		Rehabilitation	0,935	0,225	Peri- vs. Long-term recovery (*p* = 010*)			
		Long-term recovery	0,967	0,212				
		Overall	0,942	0,175	Square time effect	17,095	0.001**	0,533

†*N = 16 (13.75% replaced missing values). Marked levels of significance:* *$p < 0.05$ *and* **$p < 0.01$.

time series for each measurement day. The results are shown in **Figure 2**.

Natural oscillations of vagal activity from stronger (night) to weaker (day) are visible on all measurement days, indicated by a change of blue during the night to red during the day. Clearly, peri-operative vagal activity (T3) is severely weakened over the entire circadian cycle. In fact, on T3 a major decrease was observed even during the night, when the immune system is actually more active. During rehabilitation (T4–T6), vagal activity is gradually restored to its pre-operative circadian rhythm and to its usual circadian values. On T5 we observe a longer night time interval of strong vagal activity, which increases their average daily vagal activity. On T4–T6 we see a slight decrease between 7–9 am and 6–8 pm, most likely attributable to rehabilitation treatments. During long-term recovery (T7–T10), previously observed circadian pattern shifts to later in a day. This reduces the overall daily vagal activity, restoring the normal circadian oscillations and amplitudes, similar to pre-operative ones.

To confirm the statistical significance of these results, we performed standard ANOVA on these vagal changes and show the results in **Table 1**.

We find that the effect of the surgery on vagal activity is most significant during sleep (repeated ANOVA: part. Eta^2 [η^2] = 0.216; *Post hoc*$_{lsd}$: pre- vs. peri-operative $p = 0.004$). The vagal activity recovery after surgery is most pronounced in the 24 h mean values in the long-term recovery phase after finishing the rehabilitation (0.885 ± 0.170 peri-operative vs. 0.967 ± 0.212 long-term recovery: $\eta^2 = 0.178$; *Post hoc*$_{lsd}$: $p = 0.010$). The dynamics can also be observed in vagal activity while the patient is awake ($\eta^2 = 0.127$), but this is probably more confounded by various daily activities.

Scatter Plot Analysis

We next studied more closely how peri-operative, rehabilitation ("post-operative") and long-term recovery values of vagal dynamics depend on the corresponding pre-operative values. We investigated two specific time intervals: during the day from noon to 8 pm (when vagal activity is typically low) and during the night from 10 pm to 6 am (when vagal activity is usually strong). We averaged the values of vagal activity over these two intervals, but this time for each patient and on each measurement day separately. This provides an average daily and an average nightly vagal activity value for each patient and for each measurement day.

First, to examine the change of vagal activity due to surgery, the peri-operative vagal activity (measured on T3) was compared to pre-operative vagal activity (taken as the mean between measurements on T1 and T2). This comparison is shown as two scatter plots in top panels on **Figure 3** In both cases a reduction of vagal activity can be observed due to the surgery, especially in patients with larger pre-operative values. This is even more pronounced for the nightly values. Second, in the two middle panels in **Figure 3** we repeat the same analysis, but this time for post-operative values. They were taken as the mean between measurements on T5 and T6 (we exclude T4 from this averaging to allow more time for rehabilitation to make noticable effect), and scatter ploted agains pre-operative values (as above). Both plots show that during rehabilitation, the vagal activity values are gradually restored to the pre-operative ones. This effect is very clear during the night: patients with weaker pre-operative vagal activity show a very slow recovery, whereas patients with strong pre-operative vagal activity in fact show a noticable increase of vagal activity as a result of the early rehabilitation process. Note that due to the logarithmic representation of vagal activity values (see section "Materials and Methods"), nightly increase in vagal activity is actually much higher than immediately visible in these plots, and also higher

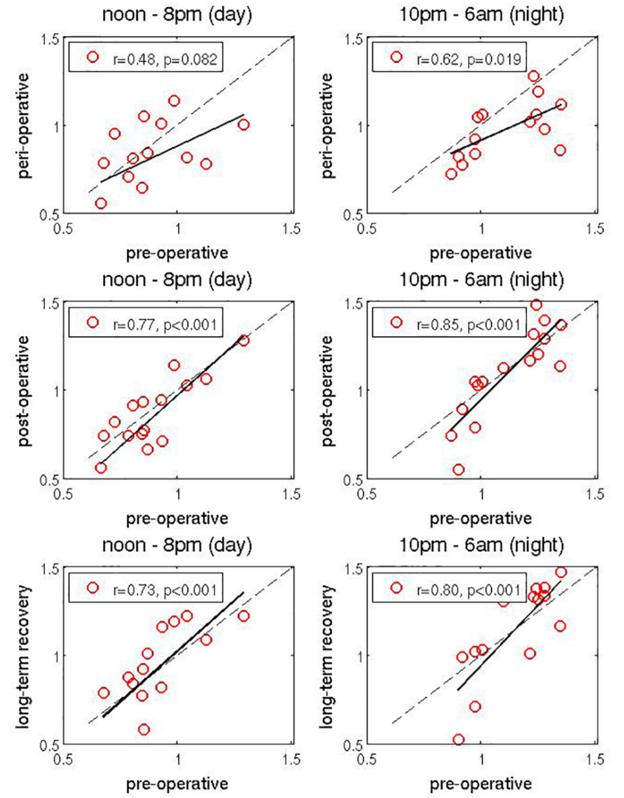

FIGURE 3 | Scatter plots of vagal activity values. Peri-operative values **(top panels)**, post-operative values **(middle panels)**, and long-term recovery values **(bottom panels)** are reported on the vertical axis, as a function of pre-operative values, which are in all panels reported on horizontal axis (each dot represents one patient). They are computed, respectively, as values on T3, average between T4 and T5, average between T9 and T10, average between T1 and T2. Changes in day-time values (measured from noon to 8 pm) are shown on the left and changes in the night-time values (measured from 10 pm to 6 am) are shown on the right. Linear regression is shown as a full black line and the line of identity is shown as a dashed black line. Correlation coefficient *r* is reported for each plot separately. Significances are all $p < 0.08$. While the event of surgery clearly reduces the vagal activity, the rehabilitation process gradually restores it to the original values. In fact, in some cases final vagal activity values are actually higher than the original pre-operative values. This effect is especially pronounced during the night (due to logarithmic representation of vagal activity values, real changes are actually more pronounced than it appears). See text and **Table 2**. Figures have different numbers of points, since for 16 patients that completed the study certain daily and/or nightly values are missing.

TABLE 2 | Statistical analysis for interaction (time × vagal-type) according (**Figures 2**, **3**).

Repeated measures ANOVA (*N* = 16) [4 × 2 design (time × vagal-type)]† logRSArr [ms]		**Vagal-type**				**Effects time vagal-type**	***F***	***P significance***	η_p^2
		Strong vagal activity (*n* = 8)		**Weak vagal activity (*n* = 8)**					
		mean	**SD**	**mean**	**SD**				
Sleep	Pre-operative	1281	0,088	1022	0,139				
	Peri-operativ	1,114	0,151	0,927	0,145	Time	4,203	0.022*	0,231
	Rehabilitation	1246	0,110	0,966	0,248	Vagal-type	13,803	0.002**	0,496
	Long-term recovery	1287	0,120	0,951	0,279				
	Overall	1,232	0,083	0,967	0,184	Interaction	1,287	0.292	0,084
Wake	Pre-operative	1,007	0,177	0,767	0,079				
	Peri-operativ	0,907	0,111	0,709	0,192	Time	2,224	0.099(*)	0,137
	Rehabilitation	1,007	0,155	0,675	0,201	Vagal-type	14,528	0.002**	0,509
	Long-term recovery	1,007	0,112	0,757	0,200				
	Overall	0,982	0,118	0,727	0,148	Interaction	1,234	0.306	0,082
Mean-24 h	Pre-operative†	**1,097**	**0,125**	**0,863**	**0,066**				
	Peri-operativ	0,986	0,109	0,783	0,162	Time	3,273	0.048*	0,190
	Rehabilitation	1,095	0,118	0,775	0,190	Vagal-type	17,151	0.001**	0,551
	Long-term recovery	1,089	0,111	0,844	0,222				
	Overall	1,067	0,090	0,816	0,146	Interaction	1,141	0.336	0,075
	Time					Time	4,432	0.042*	0,869
MANOVA	Vagal-typ					Vagal-type	5,208	0.016*	0,566
	Interaction (Time × vagal-type)					Interaction	5,900	0.021*	0,898

†*A median split of pre-operative vagal activity was used to classify into vagal-types with strong of weak vagal activity (cut-off value: 0.9654). This classification was also used for **Figure 5**. *p < 0.05 and **p < 0.01.*

than the decrease for the patients with low pre-operative vagal activity. Third, in the bottom panels of **Figure 3** we scatter plot the long-term recovery values against pre-operative values. The former were taken as the mean between T9 and T10 (again, we exclude T7 and T8 from averaging to give more time to long-term recovery). We find a generally positive slope of the regression line, indicating overall improvement of the vagal activity (recall that the logarithmic representation of vagal activity is less faithful toward larger values). Again, patients with stronger pre-operative values benefit from stronger improvement, while patients with lower pre-operative values show similar or slightly weaker values. However, we must take into account here that several months have passed since the surgery, so other life factors might have influenced the vagal activity.

Table 2 shows the results of two-way ANOVA [within-factor (time-course; 4-stage), between-factor (pre-operative-vagal activity; 2-stage)] performed to detect differences (interactions) in time course among the patients. Interestingly, while the patients suffer from larger reduction of vagal activity due to surgery (top panels of **Figure 3**), patients with strong pre-operative vagal activity exhibit larger increase of vagal activity during rehabilitation (middle panels **Figure 3** and **Table 2**: repeated MANOVA: Interaction: $p = 0.021$, $\eta^2 = 0.898$), and actually finish with vagal activity values even higher than the pre-operative ones. This is the case, at least, in some patients. The multivariate significant increase of the vagal activity ($p = 0.042$, $\eta^2 = 0.869$, see **Table 2**) after surgery is dependent on the pre-operative values (time × vagal-type: $p = 0.021$, $\eta^2 = 0.898$). This is shown for individual cases later in **Figure 4**. Due to the small and heterogeneous sample of patients, this significant dependence on initial values (pre-operative) was not seen in inference statistics via univariate testing ($p > 0.292$) for the used aggregated time points.

Effects on the Entire Circadian Dynamics

Finally, we investigated the effects of surgery and rehabilitation on the entire circadian dynamics of vagal activity. To that end we selected two patients, one with a generally strong and the other with generally weak pre-operative vagal activity (see also **Table 2**). In **Figure 4** top panel, we show three circadian time series for the first patients. Both the reduction due to surgery (red) and the improvement due to rehabilitation (green) are clearly visible over almost the entire circadian cycle. During rehabilitation, the improvement is especially pronounced during the first part of the night: vagal activity increases beyond its pre-operative values. Next we examine the same time series for the second patient (with generally weak vagal activity) in **Figure 4** bottom panel. Similar patterns are found over the circadian cycle, but the improvement due to rehabilitation is now almost entirely absent. Weak pre-operative vagal activity seem to be connected to weak vagal response during rehabilitation. This again confirms that the rehabilitation process can enhance vagal activity to values higher than normal, and particularly so for the patients with

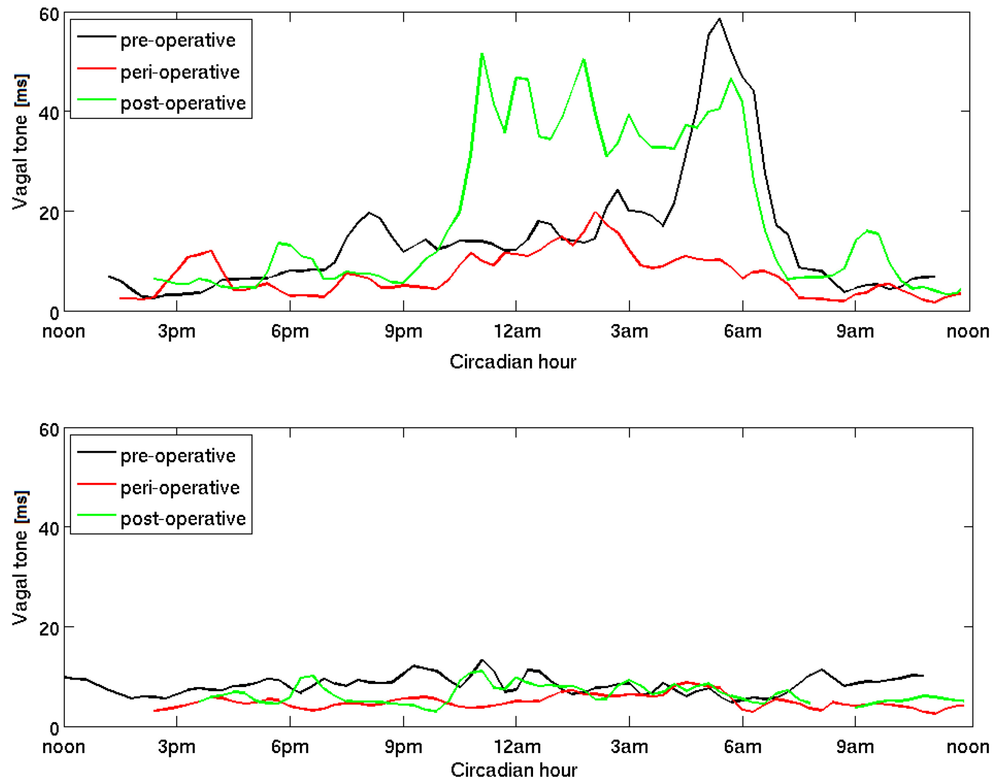

FIGURE 4 | Circadian dynamics of vagal activity (vagal tone) during the operation-rehabilitation process. A patient with a strong pre-operative vagal activity is shown in the **top panel** and another patient with a weak pre-operative vagal activity is shown in the **bottom panel**. Three circadian time series for the entire 24 h cycle are shown in each panel, measured on three specific days, pre-operative on T1, peri-operative on T3 and post-operative on T5. We remove the logarithmic scale for better clarity (see section "Materials and Methods") and use the moving average over a window of several minutes to avoid minute-to-minute fluctuation. While the patient in the **top panel** shows a clear improvement of post-operative vagal activity, especially during the night, the patient in the **bottom panel** shows very little improvement, and even during the night.

initially strong values. Our results suggest that if the patient's vagal activity could be boosted pre-operatively, this patient could realistically expect a lesser risk of peri-operative sepsis and a better outcome of rehabilitation. For completeness, we later make a clearer separation between strong and weak vagal activity.

Analysis of Other HRV Parameters

As an addition to logRSArr we next examine further HRV parameters in **Table 3** over 24 h during the examined time interval. Next to a lower vagal activity (logRSArr, $p = 0.046$) and an increased heart rate ($p = 0.072$; RR: $p = 0.011$), HRV is generally reduced immediately after surgery and it takes time to recover (only in the follow-up after rehabilitation; "long-term recovery"; all $p < 0.10$). Autonomic Balance (Ratio LF/HF) is not affected by the orthopedic surgery ($p = 0.830$).

Next we compare our patients with age and gender matched reference values from healthy controls at the pre-operative time. Results are reported in **Table 4**. Overall, patients in our clinical sample seem to have higher pre-operative heart rate ($z = 0.43$, $p = 0.096$)[2] with a slightly reduced vagal activity ($z = -0.28$, $p = 0.115$), where the other HRV values are in general similar to healthy individuals (all $p \geq 0.60$, MANOVA with HR, SDNN, TOT, LF, HF, VLF, VQ; pre-operative patients vs. healthy controls: $F = 0.674$, $p = 0.675$; see **Table 4** and **Figure 5**).[3]

Using above HRV parameters, we can now make a clearer distinction between patients with strong as opposed to weak vagal activity. To this end we perform MANOVA [calculated for HR, SDNN, TOT, LF, HF, VLF, and VQ; $F = 3.113$, $p = 0.062$, p.Eta2 = 0.675] and report the results in **Figure 5**. Patients with a pre-operative "weak vagal activity" differ markedly from patients with "strong vagal activity" in almost all HRV parameters (effect size: mean absolute z-differences[3] = 0.759, $p = 0.011$). This confirms that vagal activity (logRSArr) is a good indicator for differences in cardio-autonomic (HRV) status, as it reflects different pattern of HRV markers and thus types of cardio-autonomic profiles. It can also be useful as a marker for different reaction types, e.g., to surgery, possible complications like sepsis or different clinical courses. This also clarifies our

[2]Standard scores, also called z-values (z) are calculated by subtracting the population mean from an individual raw score and then dividing the difference by the population standard deviation (here: for healthy controls; e.g., age and gender matched reference values for autonomic (HRV) parameters see **Table 4**). Similarly, the deviations from zero or from mean-differences of z-values can interpreted as effect size as presented in **Figure 5** and **Table 4**.

[3]The data for healthy individuals were taken from a general database.

TABLE 3 | Analysis of other HRV parameters.

Heart rate variability (HRV) parameters	**Overall: $n = 16$ (24 h mean)**		**Time course (time points; 24 h mean)**				**Unifactoriell GLM – time effect**			***Post hoc* test (LSD)**
	Mean ± *SD*	**Unit**	**Pre-operative (1)**	**Peri-operative (2)**	**Rehabilitation (3)**	**Long-term recovery (4)**	***F***	***P***	η_p^2	***p* < 05**
vagal activity (logRSArr)	0,94 ± 0,17	log(ms)	0,98	0,88	0,93	0,97	3,24	0.046*	0,18	1 vs. 2; 2 vs. 4
Consecutive inter-beat intervals (RR)	788,67 ± 75,33	ms	790,49	760,15	794,48	809,56	4,16	0.011*	0,22	2 vs. 3, 4
Heart rate (HR)	78,69 ± 7,81	bpm	78,91	80,60	78,34	76,90	2,49	0.072(*)	0,14	2 vs. 4
Standard deviation of RR (SDNN)	45,65 ± 9,37	ms	49,49	40,22	46,26	46,61	5,00	0.016*	0,25	1 vs. 2
Total variability pow er (lnTOTrr)	7,11 ± 0,45	ln(ms²)	7,30	6,90	7,10	7,14	3,95	0.035*	0,21	1 vs. 2, 3
Low frequency power (lnLFrr)	5,57 ± 0,51	ln(ms²)	5,76	5,31	5,58	5,63	4,65	0.019*	0,24	1 vs. 2; 2 vs. 4
High frequency pow er (lnHFrr)	4,37 ± 0,91	ms²	4,53	4,12	4,37	4,47	2,70	0.077(*)	0,15	1 vs. 2
Very low frequency power (lnVLFrr)	6,46 ± 0,40	ms²	6,64	6,29	6,43	6,45	3,18	0.065(*)	0,17	1 vs. 2, 3
Ratio LF/HF	1,20 ± 0,60	[]	1,23	1,18	1,21	1,16	0,19	0.830	0,01	
Respiratory rate (ATMFrsa)	17,52 ± 1,29	fpm	17,02	17,64	17,46	17,95	3,19	0.062(*)	0,18	1 vs. 3,4; 3 vs. 4

Marked levels of significance: $^{(*)}p < 0.1$ and $^{*}p < 0.05$.

choice of two patiens with weak vs. strong vagal activity in earlier **Figure 4**.

Analysis of Results of Questionnaires

Further data relative to clinical information of patients (standardized questionnaires; Zerssen, 1976; Hobi, 1985; Grote, 2009) are shown in **Table 5**. Most patients report an improvement of subjective well-being (p = 0.027), already during "rehabilitation." Only in the "long-term recovery" period, the values ("well-being" and "sleep recovery") reach those of healthy reference data [0.00 ± 1.00; (z)^3]. General symptoms of "complaints" appear to be less affected over time (p = 0.139) and remain higher than in healthy controls ($z > 0.75$) throughout the whole observation period. Hence in general, no significant correlations between autonomic (HRV) parameters and questionnaire results can be observed.

DISCUSSION

Using the intensity of cardio-respiratory sinus arrhythmia for determination of vagal activity, we showed that vagal activity decreases around the time of (orthopedic) surgery, and increases during rehabilitation and long-term recovery. The former is an indicator of dangers accompanying surgical procedures, including sepsis. We found that in the wake of surgery vagal activity is impaired in essentially all patients in our sample. This impairment is present during both day and night, but is more prominent during the night. The observed decrease of vagal activity implies the breakdown of the inflammatory reflex. This hinders the ability of the body to timely resolve inflammation, thus leaving the patient considerably more vulnerable to diverse inflammatory conditions after surgery. Given that surgery and the associated tissue injury are both pro-inflammatory, preserving the inflammation resistance is paramount during this critical period. Moreover, weakening of vagal activity could be unintentionally enhanced in other ways, such as via narcotic treatments that are known to dampen ANS, including its vagal component (Shapiro et al., 2010; Tarvainen et al., 2012). Our findings suggest that caution must be observed when using such narcotics.

Our next main result is that the rehabilitation process, besides being clearly effective in restoring the vagal activity, also seems to provide a way of boosting it, as suggested by the larger than normal values observed in several patients. This vagal activity increase was particularly prominent during the night, which is normally characterized by higher vagal activity compared to the day-time values. In fact, sleep is well-known to be important for general health and helpful in many medical conditions (Reynolds et al., 2012; Moser and Kripke, 2013). Therefore, rehabilitation appears to be suited for restoring the autonomic regulation and thus the inflammatory reflex, which persist even 1 year after rehabilitation in our study.

TABLE 4 | Age and gender matched reference values for pre-operative HRV parameters.

Heart rate variability (HRV) parameters	**Healthy matched sample (n = 32)† 24 h mean**		**Rehab sample (n = 16): "pre-operative" [normalized 24 h mean; (z)]**		
	Mean ± *SD*	**Unit**	**mean [z] ± *SD***	***T***	***P***
vagal activity (logRSArr)	1, 03 ± 0, 23	log(ms)	−0, 28 ± 0, 67	−1,67	0.115
Consecutive inter-beat intervals (RR)	827, 85 ± 99, 76	ms	−0, 37 ± 0, 89	−1,69	0.112
Heart rate (HR)	75, 08 ± 9, 02	bpm	0, 43 ± 0, 96	1,78	0.096(*)
Standard deviation of RR (SDNN)	49, 64 ± 14, 68	ms	−0, 01 ± 0, 72	−0,06	0.956
Total variability power (lnTOTrr)	7, 30 ± 0, 61	ln(ms^2)	0, 00 ± 0, 70	0,02	0.982
Low frequency power (lnLFrr)	5, 83 ± 0, 72	ln(ms^2)	−0, 10 ± 0, 72	−0,53	0.604
High frequency power (lnHFrr)	4, 55 ± 0, 92	ms^2	−0, 03 ± 0, 90	−0,11	0.911
Very low frequency power (lnVLFrr)	6, 61 ± 0, 56	ms^2	0, 06 ± 0, 71	0,37	0.719
Ratio LF/HF	1, 28 ± 0, 55	[]	−0, 08 ± 1, 00	−0,33	0.747
Respiratory rate (ATMFrsa)	16, 98 ± 2, 27	fpm	0, 02 ± 0, 57	0,15	0.884

†*Age, 59.25 ± 10.34 (68.8% female).*

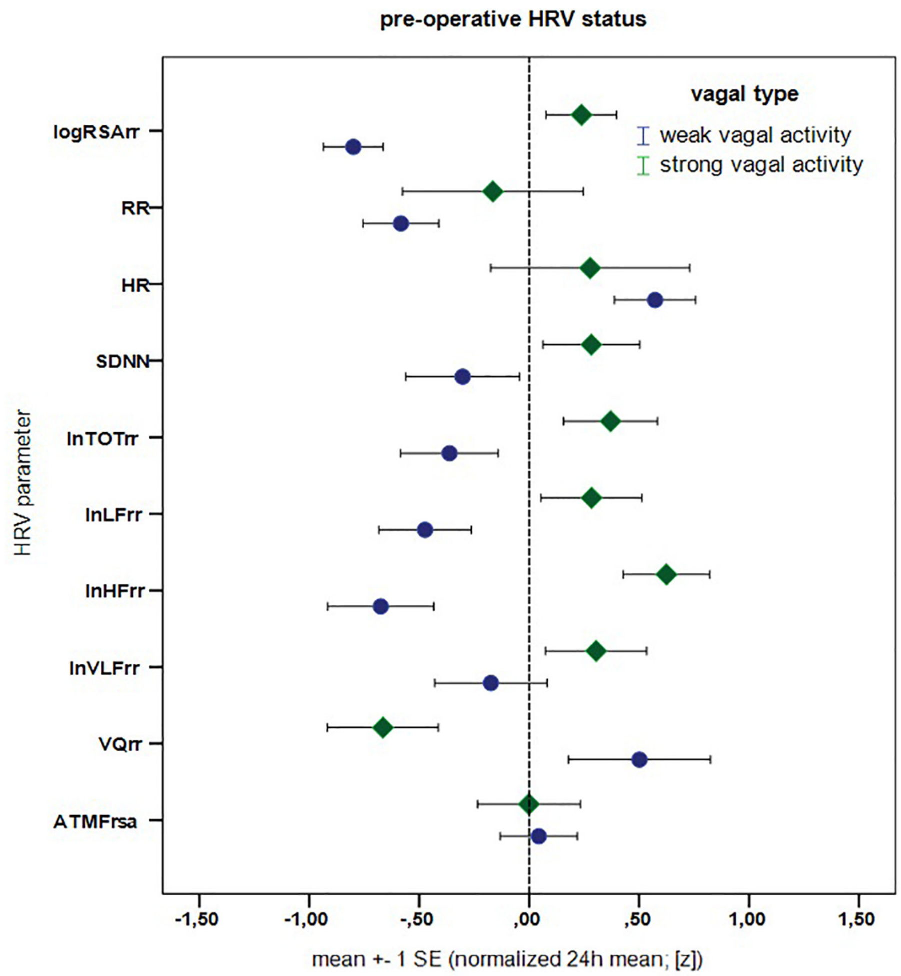

FIGURE 5 | Pre-operative cardio-autonomic status - patients with weak vs. stronge vagal activity. Mean (absolute) z-difference (weak vs. strong vagal activity) = 0.759, T = –2.936 (df = 14), p = 0.011* (MANOVA: F = 3.113, p = 0.062, η_p^2 = 0.675, calculated for HR, SDNN, TOT, LF, HF, VLF, and VQ).

TABLE 5 | Statistics and Questionnaires.

	Repeated measures ANOVA questionnaires – psychometric scales [z]†		Mean† ± *SD*	*Post hoc* (LSD; *p* ≤ 05)	*F*	*P*	η_p^2
Time course	Well-being (*n* = 13) (Hobi, 1985)	Pre-operative (1)‡	−0,426 ± 0,780	1 vs. 4	4,201	0.027*	0,276
		Peri-operativ (2)	−0,771 ± 0,879	2 vs. 3, 4			
		Rehabilitation (3)	−0,155 ± 0,852				
		Long-term recovery (4)	0,033 ± 0,686				
	Complaints (*n* = 14) (Zerssen, 1976)	Pre-operative (1)	1,094 ± 1,147		1,949	0.139	0,140
		Peri-operativ (2)	1,094 ± 1,109				
		Rehabilitation (3)	0,811 ± 1,313				
		Long-Term recovery (4)	0,753 ± 1,278				
	Sleep recovery (*n* = 13) (Grote, 2009)	Pre-operative (1)	−0,253 ± 0,995	2 vs. 4	2,391	0.086(*)	0,179
		Peri-operative (2)	−0,802 ± 1,277				
		Rehabilitation (3)	−0,258 ± 1,164				
		Long-Term recovery (4)	−0,018 ± 1,085				

*†Normalized with healthy controls [z-values]. ‡Correlation with vagal activity: r = 0.387, p = 0.155. MANOVA (n = 12) - time: F = 1.846, p-0.071(*), η_p^2 = 0.156 (Pillai). Marked levels of significance: (*)p < 0.1 and *p < 0.05.*

Vice versa of this situation has been reported. For instance, independent of the origin of inflammation, vagal activity is always reduced in inflammatory conditions (Lujan and DiCarlo, 2013). This may lead to a positive feedback loop or a vicious circle, entangling the inflammation reflex, and the accompanying pathology. Some forms of obesity are indeed known to lead to inflammation, while at the same time the chronic inflammation promotes obesity-associated diabetes (Wang et al., 2003). This indicates that besides in the development of sepsis, dysfunctional vagal control or circadian disturbance of the ANS could play a role in several key diseases of modern society, including cardiovascular diseases, metabolic syndrome and/or even development of cancer (Moser et al., 2006b; Eiró and Vizoso, 2012).

On the other hand, we realize that after surgery vagal activity is bound to increase, regardless of whether the patient undergoes rehabilitation or not. It is hard to identify which part of vagal activity increase that we observed comes as a result of rehabilitation, and which part can be attributed to natural bodily regeneration mechanisms. Yet there is extensive evidence for the positive influence of rehabilitation on a number of factors related to general well-being (Strauss-Blasche et al., 2004), many of which are directly associated with the strength of vagal activity. Our findings indicate that rehabilitation generally does have a positive effect on vagal activity, but the question of precise difference of vagal activity between patients that undergo rehabilitation and those that do not remains to be answered.

Is there a minimum value of vagal activity above which the patient is protected against diseases (such as sepsis)? While this interesting question calls for more research, we report that none of the patients contracted sepsis. This suggests that, at least for sepsis, this threshold value is below the minimums observed here.

Clinical Applications of Our Findings

We suggest that in order to reduce the chances of inflammatory conditions in the wake of surgery, it might be worthwhile to provide some activities that increase the vagal activity *prior* to the surgery ("pre-habilitation"). This would increase the patient's vagal inflammatory resistance allowing him/her to cope with the event of surgery and the associated stress more effectively (Geiss et al., 2005; Laitio et al., 2007; Mazzeo et al., 2011; Bravi et al., 2012; Bohanon et al., 2015; Ernst et al., 2017; Reimer et al., 2017; Yang et al., 2018). An additional argument in favor of this conclusion comes from our observation that patients with strong pre-surgery values make the best use of the rehabilitation in improving their vagal activity. Hence, strengthening the vagal activity of a patient during the weeks before the planned surgery appears to be a promising strategy to minimize the risk of vagal fail and hence inhibit the developement of inflammatory states. The aim of this paper was to provide more empirical evidence for these hypotheses, which if ultimately proven correct, may open new approaches, for example, in treating or preventing sepsis. This study also shows the clinical value of a quantified cardiorespiratory interactions, the respiratory sinus arrhythmia.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author MM (max.moser@medunigraz.at).

ETHICS STATEMENT

This study involved the patients from the Orthopedic Rehabilitation Center at Humanomed Center in Althofen, Austria. Patients were informed about the nature and the purpose of the study, signed the informed consent and participated voluntarily. After the study, personal results were given to all patients with adequate explanation from a doctor. The study was authorized by the Ethical Committee of the Carinthian Government, authorization number A 02/05, 01 February, 2005. All methods used in this study are in accordance with the relevant guidelines and regulations, usual for research in medical sciences.

AUTHOR CONTRIBUTIONS

MM, VG, and HP envisaged the study. HP and TO arranged for the patient voluntary participation. VG and TO carried out the measurements. MM, MF, VG, and ZL analyzed the data and the results. ZL, NG, VG, and MM wrote the manuscript. All authors reviewed the manuscript.

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Mechanische Schwingungstherapie in der Orthopädischen Rehabilitation

Evaluation stationärer Rehabilitationsmaßnahmen mit orthopädischen Patienten bei Anwendung einer mechanischen Schwingungstherapieliege

Vibration Therapy in Orthopaedic Rehabilitation

Evaluation of in-Patient Rehabilitation Measures in Orthopaedic Patients Using a Mechanical Vibration Couch

Zusammenfassung

Fragestellung. Klinische Anwendungen von mechanischen Schwingungstherapien werden widersprüchlich diskutiert. Orthopädische Krankheitsbilder, wie Endoprothesen, gelten als Kontraindikation.

Material und Methoden. Im Rahmen einer dreiwöchigen stationären Rehabilitation wurden 109 orthopädischen PatientInnen (61.4 +/- 8 Jahre) stratifiziert einer Versuchsgruppe zugeteilt: Schwingungstherapieliege (Tiktaalik), Überwassermassage (Hydrojet) und Scheinbehandlung (Placebo). Auswirkungen auf medizinische Ergebnisqualität und Herzfrequenzvariabilität wurden geprüft.

Ergebnisse. Bei einer Therapiedauer von 12 Minuten lagen die selbst wählbaren Schwingungsfrequenzen der Therapieliege zwischen 11 und 15 Hz im Brustbereich (Vibrationsschwingung) und drei bis sieben Hz im Beckenbereich (Lateralschwingung). Zwei PatientInnen mussten die Schwingungstherapie vorzeitig abbrechen (Kopfschmerz, Schwindel).

Als Folge der Mobilisierung durch die Rehabilitationsmaßnahmen kam es zu einer Zunahme der sympathikotonen Aktivierung. Es konnten Verbesserungen in Schmerzempfinden (VAS) und motorischer Funktion (Beweglichkeit, Muskelkraft) festgestellt werden. Eine Interaktion des Rehabilitationsverlauf mit den Versuchsgruppen wurde unmittelbar zu den Therapieeinheiten beobachtet: Die Beweglichkeit, Muskelkraft und Wachheit nahm in der Tiktaalik-Gruppe stärker zu. Dabei zeichnete sich mechanische Schwingungstherapie insbesondere durch eine stärkere parasympathische Aktivierung aus - es kam in der Nachruhephase zu einer signifikant stärkeren Entspannung.

Diskussion und Schlussfolgerung. Die Studienergebnisse zeigen, dass eine mechanische Schwingungsbehandlung im Liegen eine Erweiterung des bestehenden Therapieangebots in der orthopädischen Rehabilitation darstellt.

Schlüsselwörter. Orthopädie, Rehabilitation, Herzfrequenzvariabilität, Schwingungsliege, Whole Body Vibration (WBV)

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Abstract

Purpose. Clinical uses of mechanical whole body vibration therapies are the subject of contradictory debate. Orthopaedic pathologies, including the presence of endoprostheses, are considered to be contraindications.

Materials and Methods. Within the context of a 3-week in-patient rehabilitation programme 109 orthopaedic patients (61.4 +/- 8 years) were stratified to one of the trial groups: vibration therapy couch (Tiktaalik), dry water massage (Hydrojet) and sham treatment (placebo). Effects on the quality of medical results and heart rate variability were examined.

Results. The therapy had a duration of 12 minutes. The vibration frequency of the treatment couch was self-selectable between 11 and 15 Hz in the chest region and 3 and 7 Hz in the pelvic region. Two patients had to stop the vibration therapy early (headaches, dizziness).

The rehabilitation measures allowed mobilisation, leading to increased activation of the sympathetic nervous system. Improvements in pain perception (VAS) and motor function (flexibility, muscle strength) were identified during the course of the rehabilitation. An interaction of the rehabilitation process with the trial groups was observed immediately after each unit of therapy: The flexibility, muscle strength and alertness improved more markedly in the Tiktaalik group. At the same time the mechanical vibration therapy distinguished itself particularly by more marked parasympathetic modulation - there was significantly greater relaxation in the post-treatment rest phase.

Discussion and Conclusions. The study results show that mechanical vibration therapy represents an addition to the currently available treatment options for orthopaedic rehabilitation.

Key words. Orthopaedics, rehabilitation, heart rate variability, vibration couch, whole body vibration (WBV)

Trailer

Im Wechselspiel zwischen Aktivität und Erholung werden Bedingungen für einen erfolgreichen Genesungsprozess geschaffen. Voraussetzung für erfolgreiches Wirken sind evidenzbasierte Therapieanwendungen und klinische Prüfungen. Mittels mechanischer Schwingungen lässt sich Stoffwechsel und (Muskel-)Aktivität des menschlichen Organismus beeinflussen. In diesem Beitrag wird eine mechanische Schwingungstherapie sowie deren Auswirkungen für orthopädische Rehabilitanden vorgestellt.

Einleitung

Bei Erkrankungen des Bewegungsapparates muss häufig ein künstliches Gelenk eingesetzt werden. Ein wesentlicher Anteil der Anschluss- bzw. Heilbehandlungen erfolgt nach Prothesenimplantationen - im Rahmen einer stationären Rehabilitation. Dafür steht ein breites rehabilitationsmedizinisches Therapieangebot zur Verfügung, welches klare, nachhaltige Erfolge in medizinischen Scores verzeichnet [1-4], mit teilweise eindrucksvoller zeitlicher Dynamik [5,6]. Vielversprechende neue Behandlungsansätze ergänzen dabei Altbewährtes und ermöglichen es, medizinische Maßnahmen weiter zu optimieren. Klinische Prüfungen spielen hierfür eine wichtige Rolle, um evidenzbasierte Entscheidungen zu treffen bzw. die eingesetzten Therapien und Entwicklungen, wie den Einsatz von mechanischen Schwingungen im Rahmen von Bewegungs-, Trainingstherapien und Heilmassagen, medizinisch zu bewerten.

Mechanische Schwingungstherapie im klinischen Einsatz

Mittels mechanischer Schwingungen lässt sich der menschliche Organismus hinsichtlich Stoffwechsel, Zirkulation und (Muskel-)Aktivität beeinflussen, was zu einer Verbesserung des Funktions-, Bewegungs- und Kraftniveaus führen kann. Schwingungstraining und -therapie (vgl. Mechanotransduktionstherapie [7]) finden überwiegend auf Vibrationsplattformen im Stehen statt, unter dem Einsatz von vertikalen Schwingungsreizen. Die Vibrationsplatten arbeiten dabei nach einem „Hubprinzip" (die gesamte Platte wird vertikal beschleunigt) oder „Wippprinzip" (seitenalternierend) im aufrechten Stand oder in Beugeposition [8]. Über den Einsatz von horizontalen Schwingungsreizen wird in der aktuellen Fachliteratur seltener berichtet [9,10], obwohl in Abhängigkeit von Schwingungsmodalität (vertikal vs. horizontal) und Körperlage, unterscheidbare muskuläre und osteogene Wirkungen festgestellt werden können [11-14]. Ergebnisse zu Anwendungen in liegender Position, häufig in Kombination mit Kipptischanwendungen, sind die Ausnahme. Bei Liegegeräten wird durch eine exzentrische Schwingungsstimulation der Rücken und separat der Beinbereich des/der Patienten/in mechanisch bewegt. Die Muskulatur reagiert reflektorisch auf die biomechanischen Schwingungsreize.

Klinische Erfahrungen mit mechanischen Schwingungstherapien werden in der Fachliteratur widersprüchlich diskutiert und es wird allgemein ein Bedarf an weiteren Studien genannt [15-18]. Die meisten wissenschaftlichen Arbeiten sind in Bereichen der Prävention, Geriatrie, Neurologie bzw. Sport- und Trainingswissenschaften angesiedelt und können unter dem Suchbegriff „whole-body-vibration (WBV)" in den Datenbanken abgefragt werden. Es wird über eine optimierte Regeneration nach körperlichem Training [7,19-21], eine gesteigerte Muskelfunktion [22-24] und ein verbessertes Gleichgewicht [25-31] berichtet. Häufige klinische WBV-Anwendungen mit orthopädischen Hintergrund sind v.a. bei älteren PatientInnen und Frauen mit Osteoporose, Arthritis, Frakturen, Rücken-/Hüft-/Kniebeschwerden, neurologischen Erkrankungen oder Schmerzen zu finden, um die neuromuskuläre Leistungsfähigkeit, Stabilität und Mobilität positiv zu beeinflussen [8,32-39].

Neben einer zufriedenstellenden Sicherheit, werden einer Schwingungstherapie damit in der Fachliteratur potentielle positiven Einflüssen auf Beweglichkeit, Schmerzempfinden, Knochen-, Muskelfunktion und Stoffwechsel attestiert. So zeigen PatientInnen mit orthopädischen Erkrankungen, dass ein mit mechanischen Schwingungen kombiniertes Training zu besserer posturaler Kontrolle führt als ein konventionelles Vorgehen

[40,41]. Diese Ergebnisse entsprechen auch den Erfahrungen am Studienzentrum (Humanomed Zentrum Althofen).

Spezifische Merkmale von orthopädischen Rehabilitanden (z.B. Arthrose, Implantate, Operationen) werden jedoch bei Vibrationsanwendungen (z.B. Galileo®, Nemes™, Power Plate®) häufig als Kontraindikationen angeführt [14] und finden in der Regel in aufrechter Körperhaltung statt.

Exkurs: Bedeutung der Herzfrequenzvariabilität für die medizinische Bewertung

Das Herz ist durch den Sinusknoten autonom tätig, wobei die Herzaktionen durch efferente Herznerven des Autonomen Nervensystems modifiziert werden. Die Schwankungen des Schlagrhythmus reflektieren die parasympathische und sympathische Beeinflussung des Sinusknotens. Dies verleiht der Herzrate ihre typische zeitliche Struktur, die als Herzratenvariabilität (HRV) messbar wird. Eine Analyse der HRV, der Fluktuation der zeitlichen Abstände der Herzschläge, kann daher Aufschluss über die zugrunde liegende Aktivität des Autonomen Nervensystems (ANS) geben [42]. Je langsamer die Herzfrequenz bzw. je höher die parasympathische Aktivität, desto größer ist die Lebenserwartung [43-45]. Neben den bekannten Aufgaben des ANS als Koordinator von Energie- & Hormonhaushalt bzw. der Aufrechterhaltung von Vitalfunktionen gibt es direkte Zusammenhänge zwischen vegetativem Tonus und Entzündungsgeschehen [46-48] und Knochenwachstum [49].

Fragestellung

Ziel der vorliegenden Arbeit ist die Evaluation einer Schwingungstherapieliege hinsichtlich medizinischer Wirksamkeit und Sicherheit - im Kontext einer dreiwöchigen stationären orthopädischen Rehabilitation. Ein in der Fachliteratur noch wenig beachtetes Vibrationsprotokoll mit überwiegend horizontalen Schwingungsreizen wird in entspannt liegender Haltung in seinen Auswirkungen auf vegetatives Nervensystem und orthopädisch-medizinisch relevanten Zielgrößen untersucht. Im Fokus stehen Sofort- und unmittelbare Folgewirkungen der klinischen Schwingungsanwendung, welche sich u.a. vorteilhaft auf darauffolgende rehabilitationsmedizinische Therapieangebote auswirken sollte.

Methode

Studiendesign

Bei der gewählten Studienplanung handelte es sich um ein Messdesign mit Messwiederholung auf einem bis drei Faktor/en. Zwischensubjektfaktoren sind die Versuchsgruppe [Group; 3-fach gestuft; **HY**drojet vs. **PL** (Placebo) vs. **TI**ktaalik (Schwingungstherapie)] und das Beschwerdebild (4-fach gestuft; Knie vs. Hüfte vs. Schulter vs.

Wirbelsäule). Alle drei Studienbedingungen finden in passiv liegender Körperhaltung statt, um so eine Vergleichbarkeit, v.a. hinsichtlich der HRV-Analyse, zu gewährleisten. Messwiederholungsfaktoren (Innersubjektfaktoren) sind der stationäre Rehabilitationsverlauf (2-fach gestuft; Aufnahmeuntersuchung zu Beginn vs. Schlussuntersuchung nach dreiwöchiger stationärer Rehabilitation) und die Therapieeinheiten (4-fach gestuft; 1. vs. 3. vs. 6. vs. 8. Therapieeinheit). Außerdem gab es zu den Therapieeinheiten in allen drei Versuchsgruppen immer eine standardisierte Vor- und Nachruhe, die ebenfalls als Innersubjektfaktor „Therapiesetting" (3-fach gestuft; Vorruhe vs. Therapie vs. Nachruhe; jeweils 12 Minuten Dauer) - insbesondere bei der HRV-Analyse - in die physiologisch-statische Bewertung eingeht.

Messgrößen

Primäre Zielgrößen waren [50]:

- Beweglichkeit [ROM (Range of Motion); gemittelt Flexion/Extension, aktiv]: z-Normierung aller Personen & Messungen innerhalb eines Beschwerdebildes,
- Muskelkraft (MK, fünf-stufig, gemittelt Streckung/Beugung): z-Skalierung aller Messungen, jeweils für die Beschwerdebilder Knie oder Hüfte und
- Schmerz (VAS): Visuelle Analogskala mit Wertebereich von 0-10.

Als sekundäre Zielgrößen wurden cardio-vegetative Kennwerte der HRV [Herzrate, Vegetativer Quotient (LF/HF ratio), Vagustonus (logRSA [51]) und Gesamtvariabilität (lnTOT)], potentielle Nebenwirkungen (NW; Adverse Events, AE) der TIKTAALIK-Liege, Gehtests (10m Gehtest und Timed up & go) und allgemeine Kennwerte zu Befinden (Basler Befindlichkeits-Skala, BBS [52]), der Gesundheitsfragebogen (EuroQol/EQ5D [53]), der Health Assessment Questionnaire (HAQ) und der Staffelstein-Score [54,55] erhoben.

Die kontinuierliche physiologische Messung der HRV erfolgte mit dem ChronoCord® (Human Research, Weiz, Austria, Abtastrate: 8000 Hz, Auflösung 16 Bit), das aufgrund seiner Spezifikationen auch hochgenaue Analysen von HRV-Änderungen zulässt [56]. Die Analyse der HRV in der Zeit- und Frequenzdomäne erfolgte nach den Standards der Task Force [57], um Rückschlüsse auf die cardio-vegetative Regulation ziehen zu können.

Hypothesen

1. Im Rehabilitationsverlauf werden signifikante Änderungen in standardisierten klinischen und cardio-vegetativen Kenngrößen von Aufnahmeuntersuchung zu Abschlussuntersuchung festgestellt.

2. Spezifische Therapieerfolge (Gruppenunterschiede) sind unmittelbar zu den Therapieeinheiten bzw. im Messverlauf zu beobachten, wobei sich insbesondere die Schwingungstherapie positiv abhebt.

Ablauf

Einschlusskriterien waren ein operativer Eingriff oder Beschwerden am Stütz- und Bewegungsapparat (Knie, Hüfte, Schulter, Wirbelsäule), Alter zwischen 50 und 80 Jahren (Frauen nur postmenopausal), stationärer Aufenthalt bzw. Rehabilitationsbeginn nach der dritten postoperativen Woche. Ausschlusskriterien waren klinisch festgestellte Komplikationen (wie Thrombose, Lungenembolie und Wundheilungsstörungen), Herzschrittmacher, schwere KHK oder HRST, Gravidität, dialysepflichtige PatientInnen oder schwere bekannte Nausea und zerebrale Gleichgewichtsstörungen.

Nach schriftlicher Einwilligung erfolgte die Gruppenzuteilung anhand einer einfach verblindeten Stratifizierungsliste, welche Altersgruppe, Geschlecht und Beschwerdebild berücksichtigte. Anschließend fanden erste studienspezifische Messungen statt. Die StudienteilnehmerInnen in den drei Versuchsgruppen erhielten acht zusätzliche Therapieeinheiten (vgl. Tab. 1) zum üblichen rehabilitationsmedizinischen Therapieangebot einer stationären Rehabilitation für Erkrankungen des Stütz- und Bewegungsapparates:

- „Hydrojet": Überwasser-Massage im Liegen (Wärmetherapie, Wassermassage)
- „Placebo": Entspanntes Liegen auf einer inaktiven Therapieliege mit Motorengeräusch
- „Tiktaalik": Horizontale Ganzkörper-Schwingungstherapie im Liegen

Die weiteren Datenerhebungen zu Therapieeinheiten und Abschlussuntersuchung erfolgten zu konstanten Tageszeiten und sind schematisch in Abbildung 1 ersichtlich.

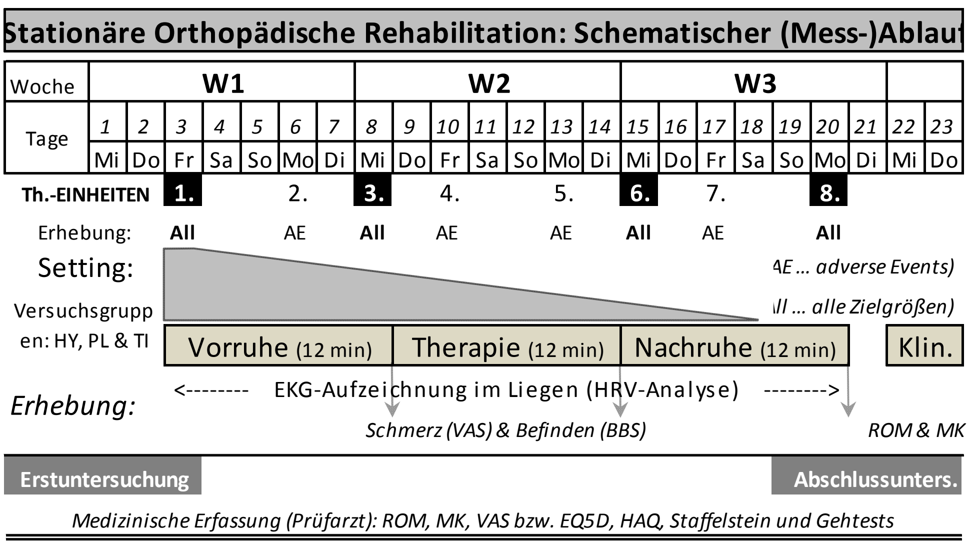

Abbildung 1: Schematischer Ablauf - Messplan.

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Die Datenerhebung betrug ein Jahr (2014-2015).

Einhaltung ethischer Richtlinien

Alle PatientInnen gaben ihr schriftliches Einverständnis vor Studienaufnahme und erhielten keine (monetäre) Entschädigung für ihre Teilnahme. Die Studie wurde von der Ethik-Kommission bzw. den zuständigen Gesundheitsbehörden bewilligt (Votum der Ethikkommission des Landes Kärnten vom 01.09.2014; Protokollnummer: A11/14 bzw. BASG-Nr.: INS-621000-0655, EUDAMED-Ref.nr.: CIV-AT-15-02-013172).

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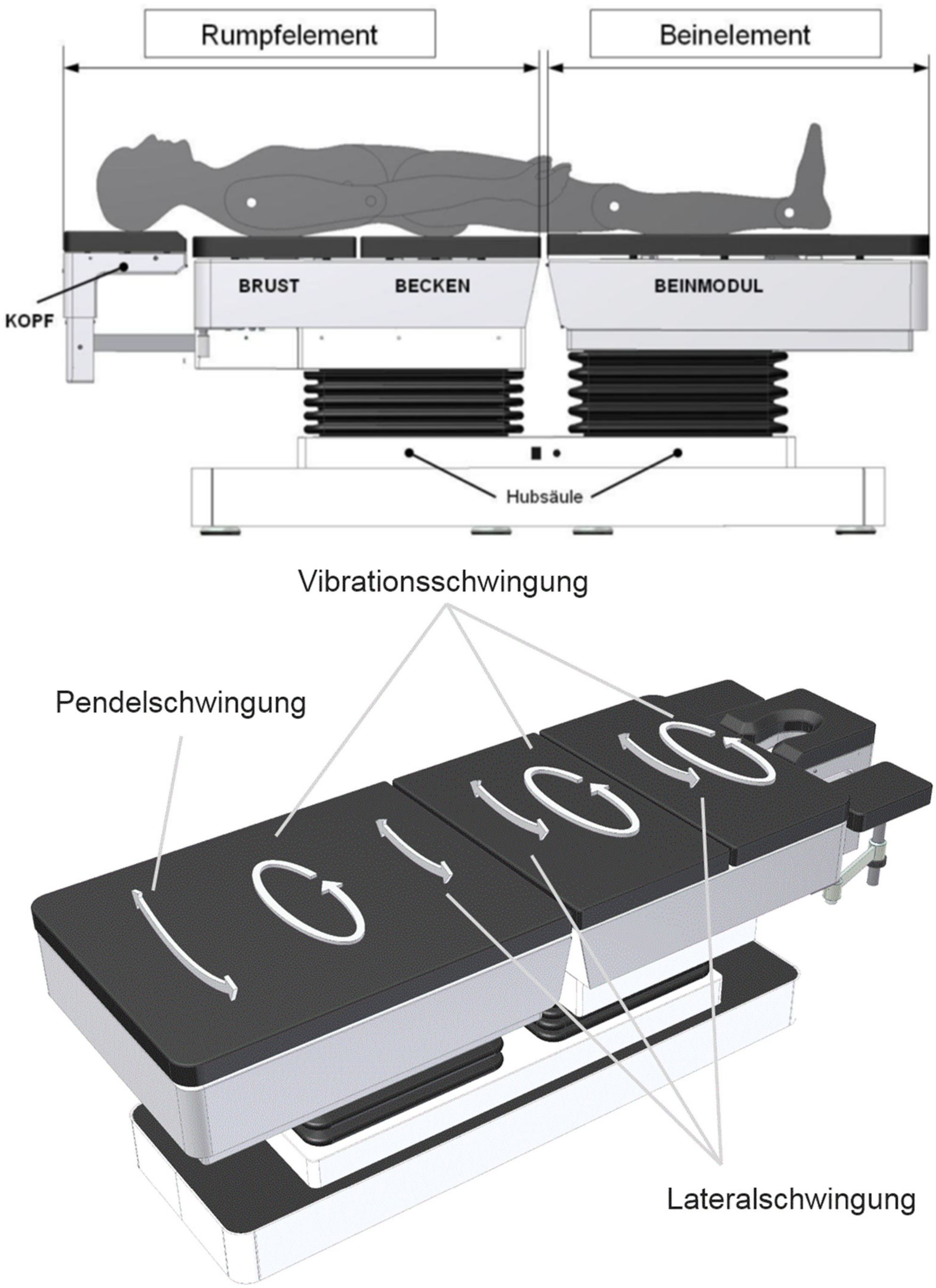
Die vorliegende Studie wurde finanziell vom MP-Hersteller der Schwingungstherapieliege-Tiktaalik (MAI International GmbH, Feistritz/Drau) unterstützt.

Prüfprodukt – Medizinprodukt: „Therapiesystem TIKTAALIK"

Das Therapiesystem besteht aus einem Rumpf- und einem Beinelement, welche einzeln stufenlos in der Höhe verstellbar sind. Außerdem können beide Elemente unabhängig voneinander jeweils bis maximal 12° in beide Richtungen (Drehachse = Breitenachse) gekippt werden. Das Kopfmodul kann sowohl in der Länge als auch in der Höhe verstellt werden. Das Therapiesystem besitzt je zwei Schwingungsarten („Vibrationsschwingung", 10 bis 26 Hz und „Lateralschwingung", 2-12 Hz") pro Modul (Brust-, Becken-, Beinmodul; vgl. Abb. 2). Im Beinmodul kann zusätzlich eine weitere Schwingungsart („Pendelschwingung", 1-1,5 Hz) aktiviert werden. Die Schwingungsauslenkung beträgt 1,5 bis 3,5 mm bei der Lateralschwingung und 25 mm bei der Pendelschwingung. Während der gesamten klinischen Studie wurden zwei der oben genannten Schwingungsmöglichkeiten aktiviert. Im Brustbereich wurde die Vibrationsschwingung und im Beckenbereich wurde eine Lateralschwingung mit 1,5 mm Auslenkung verwendet. Die mechanische Schwingungsbehandlung dauerte 12 Minuten. In Rücksprache mit dem/der Patienten/in wurde bei der ersten Therapiesitzung mit der TIKTAALIK-Liege eine individuell passende Schwingungsfrequenz für beide Schwingungsarten mit dem/der PatientIn und dem/der Prüfarzt/in gemeinsam ausgewählt. Die Einstellungen wurden für die Dauer der stationären Behandlung innerhalb einer Person konstant gehalten. Die Mehrheit der Rehabilitanden in der Tiktaalik-Versuchsgruppe wählten eine Frequenz von 11-15 Hz im Brustbereich (Vibrationsschwingung) bzw. eine Frequenz von 3-7 Hz im Beckenbereich (Lateralschwingung). Die Frequenzmodulation betrug bei beiden Schwingungen etwas unter einem Hz. Es konnten keine unterschiedlichen TIKTAALIK-Einstellungen zwischen den untersuchten vier Beschwerdegruppen festgestellt werden (alle p>.59).



Tiktaalik - Studien Version 2014-2015					
2 Elemente	**Vibration**	Ampl.	**Lateralschwingun**	Ampl.	möglich wäre ...
1. Brust	11-15Hz	<1 mm			*10-26 Hz Vibration*
2. Becken			3-7 Hz	1.5 mm	*2-12 Hz lateral*
Frequenzmodulation < 1 Hz; Beinmodul inaktiv [Pendelbewegung möglich: 1-1.5 Hz, 25 mm Auslenkung];					

Abbildung 2: Aufbau & angewendete Schwingungsarten des Therapiesystem TIKTAALIK.

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Stichprobe

Von insgesamt 109 aufgenommen StudienteilnehmerInnen (56 Männer & 53 Frauen; 61.4 +/- 8 Jahre; 28 PatientInnen mit Beschwerdefokus auf Knie, 25 auf Hüfte, 27 auf Schulter und 29 auf Wirbelsäule) sind sieben PatientInnen vorzeitig aus der Studie ausgestiegen (Dropout: 6.4%). Davon brachen zwei PatientInnen die Studie auf Grund unerwünschter Nebenwirkungen der Schwingungstherapie (Kopfschmerz bzw. Schwindel; vgl. Flussdiagramm, Abb. 3).

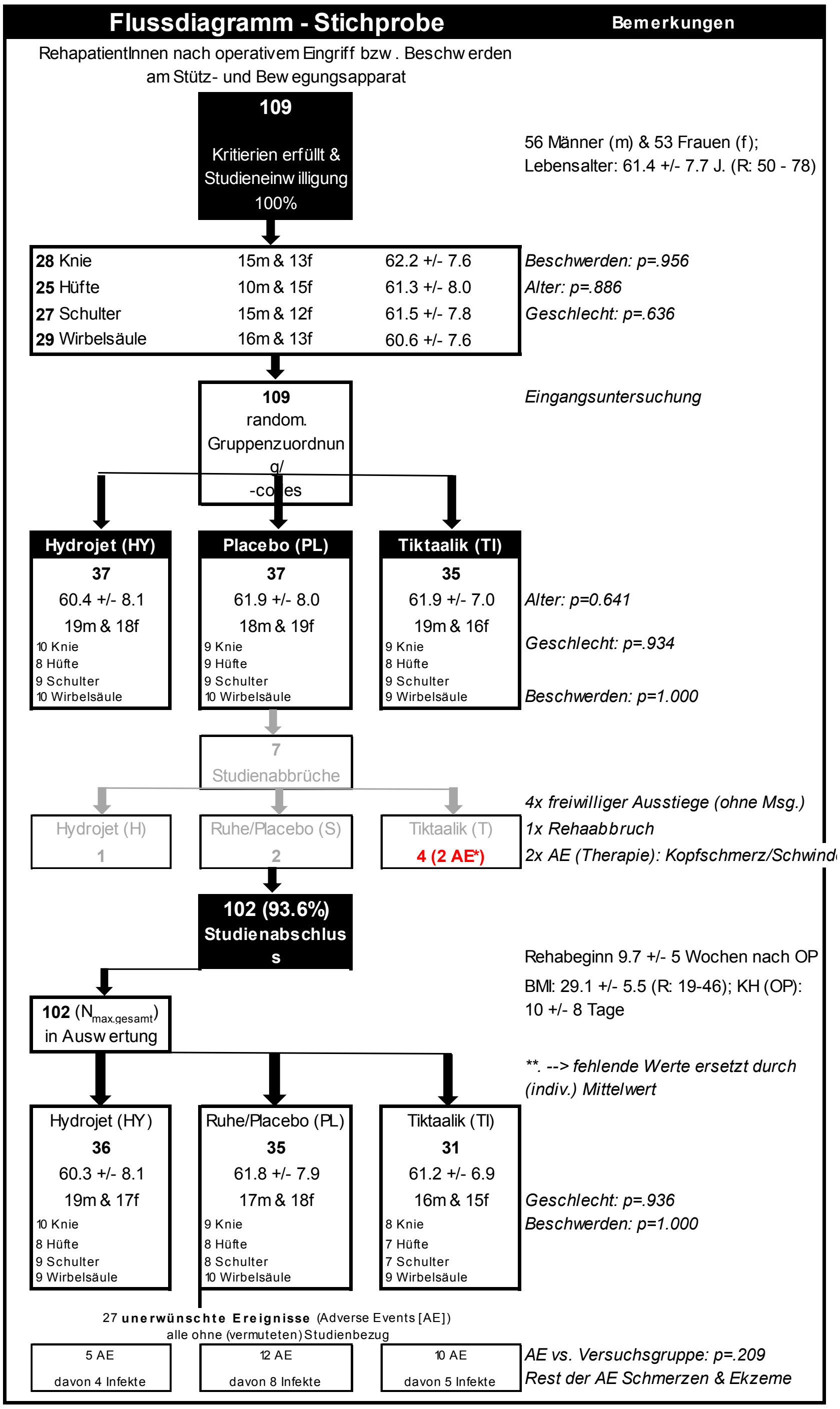

Abbildung 3: Flussdiagramm - Stichprobenbaum.

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Ergebnisse

Bei der statistischen Analyse kamen mehrfaktorielle Varianzanalysen für Messwiederholungen [(M)ANOVA; Zwischensubjekteffekte: Versuchsgruppe (3) & Gelenk (4), Innersubjekteffekte: Rehaverlauf (2 bzw. 4) & Therapiesetting (3)] zum Einsatz. Die Berechnungen erfolgten mit SPSS (Version 22). Von besonderem Interesse in dieser klinischen Prüfung ist die Abhängigkeit (Wechselwirkung) von Rehaverlauf (Zeit) x Versuchsgruppe (Group). Einzelne fehlende Werte wurden für die statistische Analyse (Messwiederholungsdesign) automatisiert durch den individuellen Gesamtmittelwert ersetzt.

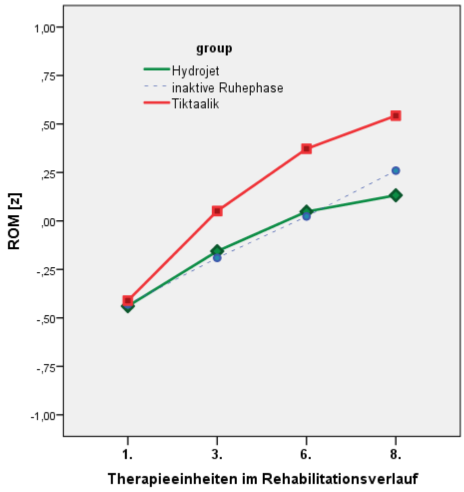
Klinische Parameter zur Ergebnisqualität

Schmerzen (VAS), Beweglichkeit (ROM, Range of Motion) und Muskelkraft verbessern sich von Rehabeginn (Aufnahme) zu Rehabilitationsende (Entlassung; vgl. Tab. 1, alle p<.01**; ebenso Kennwerte des EuroQol, Gehtests, Staffelstein und HAQ – nicht dargestellt). Die Versuchsgruppe spielt hierfür keine entscheidende Rolle (Zeit x Group: alle p>.20). In Abhängigkeit vom orthopädischen Beschwerdebild (Knie, Hüfte, Schulter, Wirbelsäule) bestehen unterschiedliche Ausprägungen in den Messgrößen bzw. können unterschiedliche Genesungsverläufe festgestellt werden (Zwischensubjekteffekt: Gelenk bzw. Interaktion: Zeit x Gelenk, p<.05*; nicht vorgestellt).

Tabelle 1: Klinische Aufnahme- und Entlassungswerte.

Kennwert	(Erfassung zu) **Aufnahme und Entlassung**								
	Gruppe	**TI**	**HY**	**PL**	**ALL**		**Innersubjekteffekte**		
	Messzeitpunkt	*MW*	*MW*	*MW*	*MW*	*SD*	Gruppe (3) x Gelenk (4) x Zeit (2)		
Schmerz (VAS) [0-10]	**n**	31	36	35	102			**Zeit**	**Zeit x Group**
	Aufnahme	**2,87**	**3,68**	**3,39**	**3,33**	2,15	**F**	92.93	1.44
	Entlassung	**1,74**	**1,95**	**1,63**	**1,78**	1,61	**p**	**.000****	.241
	Differenz gesamt	*-1,54*		*CI 95%: -1,85 bis -1,22*			**Eta²**	.508	.031
Beweglichkeit [ROM, z]	**n**	22	27	25	74			**Zeit**	**Zeit x Group**
	Aufnahme	**-0,62**	**-0,41**	**-0,60**	**-0,54**	1,06	**F**	243.8	0.93
	Entlassung	**0,40**	**0,41**	**0,34**	**0,39**	0,83	**p**	**.000****	.398
	Differenz gesamt	*0,94*		*CI 95%: 0,82 bis 1,06*			**Eta²**	.789	.028
Muskelkraft [z]	**n**	15	18	17	50			**Zeit**	**Zeit x Group**
	Aufnahme	**-0,51**	**-0,44**	**-0,29**	**-0,41**	0,82	**F**	13.13	0.05
	Entlassung	**-0,08**	**-0,05**	**0,08**	**-0,02**	0,86	**p**	**.001****	.950
	Differenz gesamt	*0,39*		*CI 95%: 0,17 bis 0,60*			**Eta²**	.230	.002

Ebenso zeigen sich kontinuierliche Verbesserungen unmittelbar zu den einzelnen Therapieeinheiten in den klinischen Messgrößen (vgl. Tab. 2; alle p<.01**). Hierbei fällt auf, dass sich die TI-Gruppe hinsichtlich Beweglichkeit (Rehaverlauf x Group: p=.003**) und Muskelkraft (p=.035*) signifikant besser entwickelt als die beiden anderen Gruppen (vgl. Tab. 2 & li. Abb. 4). Diese Beobachtung gilt für die klinische Evaluation unmittelbar nach einer Therapieeinheit (vgl. Abb. 1).



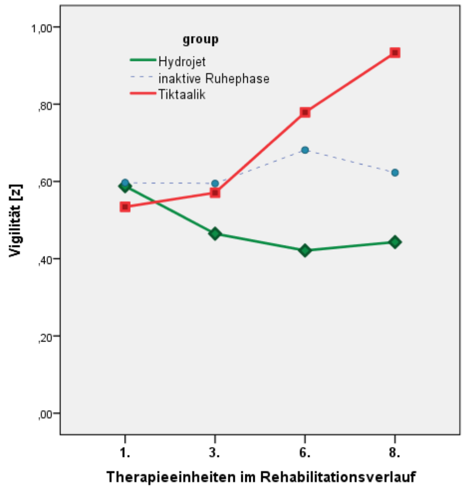


Abb. 4: Therapieeinheit und Beweglichkeit (ROM; li.) bzw. Vigilität (re.).

Bei den Therapiesitzungen erkennt man ebenfalls eine fortschreitende Befindensverbesserung (p=.012*; Anmerkung v.a. bei der Dimension „Vitalität"; nicht dargestellt). Bei der Skala „Vigilität" kann eine signifikante Wechselwirkung zwischen Verlauf x TI vs. HY-Gruppe beobachten werden (p=.020*; vgl. re. Abb. 4).

Tabelle 2: Unmittelbare Therapiewirkungen in klinischen Kennzahlen.

Kennwert	(Erfassung zu) **Therapieeinheit**								
	Gruppe	**TI**	**HY**	**PL**	**ALL**		**Innersubjekteffekte**		
	Messzeitpunkt	*MW*	*MW*	*MW*	*MW*	*SD*	Gruppe (3) x Gelenk (4) x Zeit (4)		
Schmerz (VAS) [0-10]	**n**	31	36	35	102			**Zeit**	**Zeit x Group**
	1. Einheit	**2,71**	**3,19**	**2,61**	**2,84**	1,86	**F**	10.65	1.06
	3. Einheit	**2,16**	**3,31**	**2,56**	**2,70**	1,93	**p**	**.000****	.387
	6. Einheit	**2,34**	**2,73**	**2,07**	**2,39**	1,80	**Eta²**	.106	.023
	8. Einheit	**1,72**	**2,39**	**2,04**	**2,07**	1,89			
	Diff. ges. $_{E1\ zu\ E8}$	*-0,80*		*CI 95%: -1,16 bis -*					
Beweglichkeit [ROM, z]	**n**	30	36	32	98			**Zeit**	**Zeit x Group**
	1. Einheit	**-0,41**	**-0,42**	**-0,42**	**-0,42**	0,98	**F**	120.2	3.39
	3. Einheit	**0,05**	**-0,15**	**-0,18**	**-0,10**	0,91	**p**	**.000****	**.003****
	6. Einheit	**0,37**	**0,06**	**0,04**	**0,15**	0,93	**Eta²**	.583	.073
	8. Einheit	**0,53**	**0,13**	**0,27**	**0,30**	0,93			
	Diff. ges. $_{E1\ zu\ E8}$	*0,73*		*CI 95%: 0,62 bis 0,84*					
Muskelkraft [z]	**n**	15	18	17	50			**Zeit**	**Zeit x Group**
	1. Einheit	**-0,78**	**-0,49**	**-0,37**	**-0,54**	1,09	**F**	38.1	2.35
	3. Einheit	**0,04**	**-0,08**	**0,17**	**0,04**	1,01	**p**	**.000****	**.035***
	6. Einheit	**0,57**	**0,03**	**0,57**	**0,37**	0,84	**Eta²**	.464	.096
	8. Einheit	**0,68**	**0,16**	**0,58**	**0,46**	0,85			
	Diff. ges. $_{E1\ zu\ E8}$	*1,01*		*CI 95%: 0,77 bis 1,25*					

Cardio-vegetative Parameter der Herzfrequenzvariabilität

Die HRV-Auswertung zeigt, dass der vegetative Quotient (VQ_{rr}, LF/HF ratio) als Folge der allgemeinen physischen Mobilisierung kontinuierlich im Rehaverlauf zunimmt (Rehaverlauf: p=.001**; vgl. Tab. 3). Der Vagustonus ($logRSA_{rr}$, $lnHF_{rr}$, SD1) nimmt tendenziell im Rehaverlauf etwas ab [Rehaverlauf: $lnHF_{rr}$, p=.080(*) & SD1, p=.048*; nicht dargestellt; $logRSA_{rr}$: p=.168, vgl. Tab. 3], wohingegen die Gesamtvariabilität v.a. gegen Ende der stationären Rehabilitation zunimmt [$lnTOT_{hf}$, p=.055(*), vgl. Tab. 3]. Die Herzrate zeigt einen u-förmigen Verlauf mit geringfügig höheren Mittelwerten zu Beginn und Ende der Reha (p=.025*, vgl. Tab. 3).

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Tabelle 3: Rehabilitationseffekte auf die cardio-vegetative Regulation.

Kennwert	(Erfassung im Liegen, unmittelbar zu) **Therapieeinheit**									
	Gruppe	**TI**	**HY**	**PL**	**ALL**		**Statistik - Innersubjekteffekte**			
	Messzeitpunkt	*MW*	*MW*	*MW*	*MW*	*SD*	Gruppe (3) x Gelenk (4) x Rehaverlauf (4)			
	n	30	34	33	97			**F**	**p**	**part. Eta²**
Herzrate [bpm]	1. Einheit	**72,754**	**71,875**	**72,714**	**72,432**	10,661	**Rehaverlauf**	3,165	**.025***	.036
	3. Einheit	**71,608**	**70,368**	**71,020**	**70,973**	9,798	**Rehaverlauf x Group**	0,465	.834	.011
	6. Einheit	**71,494**	**70,435**	**70,810**	**70,890**	10,322				
	8. Einheit	**73,193**	**72,135**	**71,066**	**72,099**	9,630				
LF/HF ratio (VQ_{rr}, [])	1. Einheit	**0,946**	**0,832**	**0,895**	**0,889**	0,726				
	3. Einheit	**0,916**	**0,899**	**0,928**	**0,914**	0,755	**Rehaverlauf**	5,336	**.001****	.059
	6. Einheit	**0,968**	**0,977**	**1,010**	**0,986**	0,711	**Rehaverlauf x Group**	0,319	.927	.007
	8. Einheit	**1,052**	**1,064**	**1,119**	**1,079**	0,715				
logRSA [ms]	1. Einheit	**0,986**	**0,974**	**0,976**	**0,979**	0,245				
	3. Einheit	**0,993**	**1,002**	**1,006**	**1,000**	0,253	**Rehaverlauf**	1,698	.168	.020
	6. Einheit	**1,013**	**0,987**	**0,986**	**0,995**	0,234	**Rehaverlauf x Group**	0,337	.917	.008
	8. Einheit	**0,978**	**0,946**	**0,976**	**0,966**	0,238				
Ges.var. ($lnTOT_{hf}$, ms^2)	1. Einheit	**1,842**	**1,666**	**1,877**	**1,792**	0,780				
	3. Einheit	**1,848**	**1,657**	**1,862**	**1,786**	0,798	**Rehaverlauf**	2,560	**.055(*)**	.029
	6. Einheit	**1,819**	**1,723**	**1,786**	**1,774**	0,747	**Rehaverlauf x Group**	0,998	.427	.023
	8. Einheit	**1,962**	**1,902**	**1,843**	**1,900**	0,765				

Die Versuchsgruppe spielt für die allgemeine Entwicklung in der cardio-vegetativen Regulation - ebenso wie bei den prüfärztlich erfassten klinischen Kennwerten zu Aufnahme und Entlassung - keine Rolle (Rehaverlauf x Group: p>.40, vgl. Tab. 3).

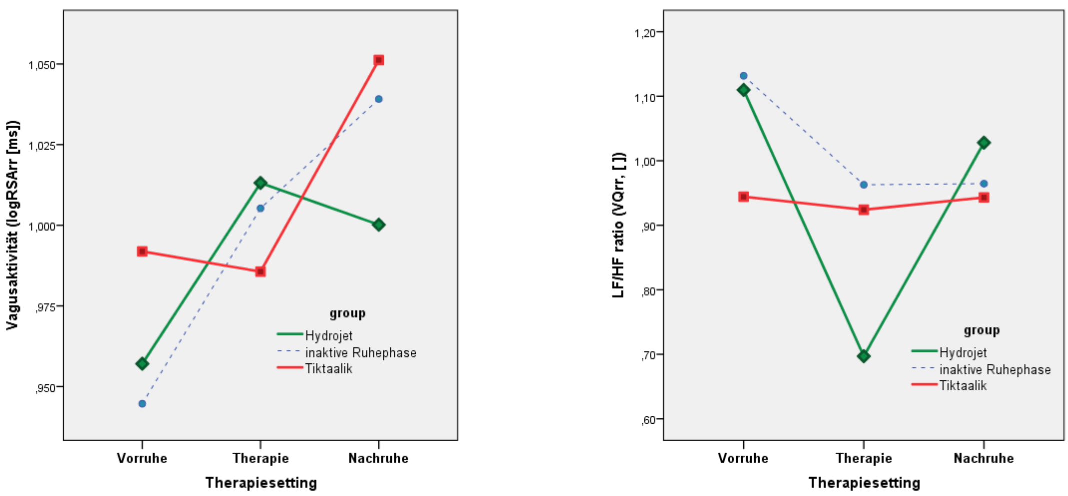

Abbildung 5: Vegetative Regulation zur Therapieeinheit (li.: logRSA, re.: LF/HF ratio).

Bei den Therapieeinheiten kommt es parallel zu einer kontinuierlich abnehmenden Herzrate zu einer kontinuierlichen Zunahme der Vagusaktivität von Vor- zu Nachruhe (Therapiesetting: alle p<.001**, vgl. Tab. 4). Nur bei der Tiktaalikbehandlung ist hier eine Stagnation bzw. mittlere Abnahme der vagalen Aktivität ($logRSA_{rr}$) unmittelbar zur Schwingungsexposition zu verzeichnen, gefolgt von einer starken Zunahme in der Nachruhephase (vgl. li. Abb. 5; Therapiesetting x Group: p=.001**, vgl. Tab. 4). Hingegen kann insbesondere während der Hydrojet-Behandlung eine merkliche Abnahme im VQ_{rr} (LF/HF ratio) beobachtet werden (vgl. re. Abb. 5; Therapiesetting x Versuchsgruppe: p=.007**, vgl. Tab. 4). Diese Senkung der vegetativen Balance (VQ_{rr}) mit anschließendem Rebound-Effekt in der Nachruhephase wird u.a. auch durch eine Abnahme der LF-Komponente (Low Frequency, p=.000**; nicht dargestellt) bzw. der TOT (Gesamtvariabilität, Therapiesetting: p=.000**; Therapiesetting x Group: p=.038*, vgl. Tab. 4) vermittelt; somit insgesamt durch eine Reduktion der autonomen bzw. sympathischen Aktivierung während der Anwendung.

Die Atemfrequenz von Vorruhe über Therapieanwendung und Nachruhe bleibt bei der Placebobedingung annähernd konstant (16,5 +/- 2,6 cpm), wohingegen sie bei den beiden anderen Therapiegruppen um ca. einen halben Atemzug pro Minute während der Therapie zunimmt (Therapiesetting x Versuchsgruppe: F=4.52, p=.002**, part. Eta^2=.096).

Tabelle 4: Unmittelbare Therapiewirkungen in der cardio-vegetativen Regulation.

Kennwert	(Erfassung im Liegen zu) **Therapiesetting**									
	Gruppe	**TI**	**HY**	**PL**	**ALL**		**Statistik - Innersubjekteffekte**			
	Messzeitpunkt	*MW*	*MW*	*MW*	*MW*	*SD*	Gruppe (3) x Gelenk (4) x Therapiesetting (3) x Zeit (4)			
	n	30	34	33	97			**F**	**p**	**part. Eta^2**
Herzrate [bpm]	Vorruhe	**73,560**	**72,250**	**73,750**	**73,160**	9,620	**Therapiesetting**	101,663	**,000****	.545
	Therapie	**72,425**	**71,517**	**71,020**	**71,629**	9,663	**Therapiesetting x Group**	5,214	**,001****	.109
	Nachruhe	**70,950**	**69,908**	**69,746**	**70,175**	9,068				
	gesamt	**72,310**	**71,225**	**71,506**	**71,656**	9,370				
LF/HF ratio (VQ_{rr}, [])	Vorruhe	**1,015**	**1,048**	**1,073**	**1,046**	0,676	**Therapiesetting**	14,864	**,000****	.149
	Therapie	**0,925**	**0,716**	**0,924**	**0,851**	0,741	**Therapiesetting x Group**	3,613	**,007****	.078
	Nachruhe	**0,991**	**1,046**	**0,984**	**1,008**	0,672				
	gesamt	**0,977**	**0,937**	**0,994**	**0,968**	0,661				
logRSA [ms]	Vorruhe	**0,975**	**0,956**	**0,938**	**0,956**	0,227	**Therapiesetting**	30,488	**,000****	.264
	Therapie	**0,967**	**0,991**	**0,991**	**0,984**	0,233	**Therapiesetting x Group**	5,091	**,001****	.107
	Nachruhe	**1,036**	**0,990**	**1,025**	**1,016**	0,216				
	gesamt	**0,993**	**0,979**	**0,985**	**0,985**	0,221				
Ges.var. ($lnTOT_{hf}$, ms^2)	Vorruhe	**1,894**	**1,795**	**1,818**	**1,833**	0,737	**Therapiesetting**	25,538	**,000****	.231
	Therapie	**1,697**	**1,487**	**1,785**	**1,653**	0,720	**Therapiesetting x Group**	2,594	**,038***	.058
	Nachruhe	**2,003**	**1,882**	**1,946**	**1,941**	0,726				
	gesamt	**1,864**	**1,721**	**1,850**	**1,809**	0,692				

Diskussion

Die Studienergebnisse zeigen, dass insbesondere für PatientInnen aus dem orthopädischen Formenkreis nach einer schweren Erkrankung oder Operation eine mechanische Schwingungsbehandlung im Liegen eine vielversprechende Erweiterung des bestehenden medizinischen Therapieangebots darstellt.

Der klinische Outcome, Kennwerte der medizinischen Ergebnisqualität zum Entlassungszeitpunkt in allen drei Versuchsgruppen sind als Erfolg des gesamten und bewährten rehabilitationsmedizinischen Therapieangebots zu bewerten, lassen jedoch keine unmittelbaren Rückschlüsse auf einzelne Therapieangebote zu (vgl. Tab. 1). Medizinische Intention war es u.a. durch bekannte Effekte der WBV-Therapie einen optimierten Status des/der PatientIn zu schaffen, der eine effizientere Durchführung von weiteren physikalisch-medizinischen Anwendungen, wie Bewegungs- & medizinische Trainingstherapien, ermöglicht. Für die Praxis relevante, unmittelbare und spezifische Auswirkungen einer horizontalen Schwingungstherapieliege auf primäre klinische Zielgrößen, wie Beweglichkeit, Kraft und Schmerzempfinden und Vegetativum konnten nachgewiesen werden (vgl. Tab. 2, Abb.

4). Aussagen zur Nachhaltigkeit der Therapieeffekte können auf Grundlage des gewählten Studienaufbaus nicht getroffen werden (vgl. Limitation).

Die kontinuierliche Zunahme des vegetativen Quotienten bzw. der autonomen Aktivierung während der stationären Rehabilitation (vgl. Tab. 3) kann als eine Reaktion und Bewältigung der erfolgten physischen Mobilisierung durch den Organismus gedeutet werden. Aus Erfahrungen der Physikalischen und Rehabilitativen Medizin [5,58,59] und Referenzprojekten des Humanomed Zentrums [6] ist bekannt, dass es mit Rückkehr in den Alltag mittel- und langfristig wieder zu einer kontinuierlichen Absenkung des vegetativen Quotienten kommt.

Die Intention der Therapiewirkungen zwischen „Hydrojet" (Muskelrelaxation) und „Tiktaalik" (Mobilisierung) sind unterschiedlich, was sich deutlich in der kardio-vegetativen Dynamik widerspiegelt. Spezifische Unterschiede, eine signifikante Interaktion des stationären Rehabilitationsverlaufs mit den drei Versuchsgruppen, werden unmittelbar zu den Therapieeinheiten festgestellt (vgl. Abb. 4 & 5 bzw. Tab. 2 & 4). Im Gegensatz zu einer Überwasser-Massage (Hydrojet-Behandlung) macht sich die Spezifität einer mechanischen Schwingungstherapie (Tiktaalik-Behandlung) - neben einer unmittelbar stärkeren Wirkung auf die funktionelle Motorik (Beweglichkeit und Muskelkraft; vgl. Tab. 2 & Abb. 4) - durch eine stärkere vagotone Modulation bemerkbar. Bei Schwingungsexposition kommt es zu einer Unterdrückung des Vagustonus. Im Anschluss an die Behandlung kann in der Nachruhephase eine signifikant stärkere autonome Entspannung beobachtet werden (vgl. li. Abb. 5). Das vegetative „Anstoßen" bzw. „Aufschaukeln" kann im Sinne eines Beanspruchungs(Reiz)-Erholungs(Reaktions)-Schemas zu positiven und nachhaltigen Therapieeffekten führen. Diese beobachtete Reiz-Reaktionsphysiologie stellt für den Organismus eine Orientierungshilfe dar. Durch die vegetative Auslenkung kommt es zu einer Stabilisierung und Stärkung von physiologischen Regelsystemen, was nachhaltig zu einer günstigeren physiologischen Körperregulation führt [5,58-60].

Aus rehabilitationsmedizinischer Sicht handelt es sich bei der physio-physikalischen Schwingungstherapie um eine Bewegungs- bzw. medizinische Trainingstherapie mit hinreichender Evidenz. Die empirisch-klinischen Erfahrungen mit mechanischen Schwingungstherapien in der Fachliteratur bzw. im eigenen Haus sind vielversprechend. Potentielle Behandlungsrisiken bzw. Nebenwirkungen können bei fachgerechter Anwendung und Betreuung als gering eingestuft werden (vgl. Abb. 3). Im Rahmen der Studie wurde bei ca. 250 Anwendungen nur zweimal die Therapie auf Grund unerwünschter Nebenwirkungen abgebrochen (Kopfschmerzen und

Schwindel). Weitere unerwünschte Ereignisse, welche unmittelbar mit der Therapieliege in Zusammenhang gebracht werden können, wurden nicht beobachtet.

Limitation

Bei der prüfärztlichen Entlassungsuntersuchung waren keine signifikanten Gruppenunterschiede festzustellen (vgl. Tab. 1 & 3). Dies war/ist jedoch nicht zu erwarten, da eine einzelne zusätzliche Therapiemaßnahme mit einer Gesamtdauer von 96 Minuten (entspricht ca. 5% der gesamt durchgeführten Therapiemaßnahmen) sich in einem Bündel von bewährten medizinischen Rehabilitationsmaßnahmen über drei Wochen (im Ausmaß von mindestens 1800 Minuten) nicht hervortun kann.

Aus ethischen, praktischen und ökonomischen Gründen kann eine klinische Rehabilitationsstudie bei orthopädischen PatientInnen der Phase II nicht ausschließlich einzelne Therapieformen/-anwendungen betrachten bzw. „reine" Kontrollgruppen beinhalten, wie dies aus wissenschaftstheoretischer Sicht eventuell wünschenswert wäre. Evidenzbasierte medizinische Forschung (und Forderungen) zur Wirksamkeit und Nachhaltigkeit einzelner Heilverfahren im stationären Rehabilitationsbereich ist daher immer ein Kompromiss, denn man kann keinem/er PatientIn etablierte und bewährte medizinische Angebote einfach vorenthalten. Die StudienautorInnen glauben jedoch mit dem gewählten Studiensetting eine zufriedenstellende Lösung gefunden zu haben. Im Gegenzug kann die externe Validität der vorgestellten klinischen Prüfung als ausreichend hoch eingestuft werden.

Fazit für die Praxis

Entsprechend der klinischen MP-Prüfung und nach aktuellem Kenntnisstand handelt es sich bei der geprüften mechanischen Schwingungsliege (Tiktaalik-Therapiesystem) um eine risikoarme Therapiemethode, die unmittelbar zu einer besseren motorischen Funktion bei orthopädischen PatientInnen in der Phase II führt und so anderen Therapieformen „zuarbeitet".

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Titelseite

Medizinische Ergebnisqualität: Unspezifische Outcome-Parameter einer stationären Rehabilitation des Stütz- und Bewegungsapparates in Österreich

Monozentrische klinische Referenzwerte eines deskriptiven Evaluationsmodells für Routine-Outcome-Measurements in Orthopädischer Rehabilitation und Gesundheitsvorsorge Aktiv

Medical quality outcomes: unspecific outcome parameters of an inpatient musculoskeletal system rehabilitation in Austria

Monocentric clinical reference values of a descriptive evaluation model for routine outcome measurements in Orthopaedic Rehabilitation and the "Health through Activity" programme

Zusammenfassung

Fragestellung: Im Rahmen der Dokumentation von Patienten, die eine stationäre Rehabilitation in Anspruch nehmen, werden obligatorisch Kennzahlen zur Medizinischen Ergebnisqualität (MEQ) standardisiert erfasst. Veröffentlichungen dazu sind jedoch noch die Ausnahme. Ziel ist die Bereitstellung von elementaren klinischen Referenzdaten und Darstellung der Veränderung bei einer stationären Rehabilitation des Stütz- und Bewegungsapparates.

Material und Methoden: Die in Leistungsprofilen von Kostenträgern geforderten Outcome-Parameter beinhalten neben krankheitsspezifischen Kennwerten auch unspezifische allgemeine Gesundheitsmerkmale, wie Körpermaße, Kreislaufparameter und gesundheitliche Beschwerden. Die Daten von 11.414 Patienten (54,7 +/- 12,3 Jahre,

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Range: 14-95; 53% Frauen), die eine Orthopädische Rehabilitation oder eine Gesundheitsvorsorge Aktiv erhielten, wurden statistisch aufbereitet.

Ergebnisse: Unspezifische Indikatoren der MEQ können zu drei Faktoren zusammengefasst werden (Varianzaufklärung 71%). Es bestehen Ausgangswertunterschiede in Abhängigkeit von Indikation und Geschlecht. Der Effekt des stationären Rehabilitationsaufenthalts ist vergleichbar. 74% der Patienten profitieren unmittelbar von der Rehabilitation. 20% der Patienten zeigen keine Änderung, 6% verschlechtern sich. Im Gegensatz zu Kreislaufkennwerten und Beschwerden bleiben anatomische Merkmale nahezu unverändert.

Diskussion und Schlussfolgerung: Im stationären Rehabilitationssetting werden Risikofaktoren bei der Mehrzahl der Patienten reduziert und das Allgemeinbefinden verbessert, wobei derartige Erfolge nicht alle Rehabilitanden erreichen. Es besteht ein Bedarf an differenzierten Behandlungspfaden, um die Erfolgsquote und die Nachhaltigkeit zu verbessern. Klinische Referenzwerte können dabei einen wertvollen Beitrag zur Qualitätssicherung und Evaluation liefern.

Schlüsselwörter: *Stationäre Rehabilitation, Medizinische Ergebnisqualität, Routine Outcome Measurement, Referenzdaten*

Abstract

Purpose: As part of the documentation for all patients who benefit from inpatient rehabilitation, standardized collection of data relating to performance indicators for medical quality outcomes (MQO) is obligatory. Publications on this subject, however, are rare. The aim is to make available elementary clinical reference data and show changes relating to an inpatient musculoskeletal rehabilitation.

Materials and Methods: The outcome parameters required by funding agencies in the service profile include, besides disease-specific parameters, unspecific general health parameters such as body measurements, circulatory parameters and health problems. Data from 11 414 patients (54.7 +/- 12.3 years, range: 14 - 95; 53% women) who had undergone orthopaedic rehabilitation or a "Health through Activity" programme, were statistically analysed.

Results: Unspecific MQO indicators can be summarized in three categories (explained variance 71%). There is variation in the initial values according to indication and gender. The effect of inpatient rehabilitation stay is comparable. 74% of patients gain immediate benefit from the rehabilitation. 20% of patients show no change and 6% get worse. In contrast to circulatory parameters and symptoms, anatomical characteristics remain practically unchanged.

Discussion and Conclusions: Inpatient rehabilitation setting reduces risk factors in the majority of patients and improves general wellbeing, although not all those having rehabilitation reach such a level of success. In order to improve the success rate and sustainability of the treatment, differentiation of treatment pathways is required. In this way, clinical reference values can provide a valuable contribution to quality assurance and evaluation.

Key words: *Inpatient rehabilitation, medical quality outcomes, routine outcome measurement, reference data*

Einleitung

In Zeiten knapper werdender Ressourcen gewinnt die Beweisführung der Wirksamkeit medizinischer Maßnahmen immer mehr an praktischer und gesundheitsökonomischer

Bedeutung. Neue Möglichkeiten der medizinischen Versorgung und sich ständig ändernde Rahmenbedingungen sind eine Herausforderung für das Qualitätsmanagement, welches anhand Struktur-, Prozess- und Ergebnismerkmalen den Grad der Erreichung vordefinierter Zielen erfasst. Direkte lineare Zusammenhänge zwischen einzelnen Qualitätsdimensionen sind nicht unmittelbar gegeben [1,2].

Rehabilitationsmaßnahmen und sekundärpräventive medizinische Programme sowie evidenzbasierte Behandlungspfade sind Gegenstand teilweise kontrovers geführter Diskussionen. Chronische muskuloskelettale Erkrankungen belasten zunehmend die Volksgesundheit. Die häufigste Ursache für YLD (*years lived with disability*) sind chronische Rückenbeschwerden [3]. Die Jahresprävalenz für Rückenschmerzen ist im Alter zwischen 40 und 69 Jahren am höchsten, Frauen sind häufiger betroffen [4,5]. Auf Basis der Gesundheitsbefragung 2014 wurde in Österreich der Anteil der Bevölkerung mit chronischen Rückenbeschwerden auf 24% bzw. 1,8 Mio. Personen geschätzt [6].

Aktuelle Behandlungspfade betonen ein stratifiziertes Vorgehen, aktive Therapien und edukative Maßnahmen, wobei Evidenz und gelebte Praxis nach wie vor deutlich auseinanderklaffen [7-10].

Im Laufe des Rehabilitationsprozesses werden vier chronologisch ablaufende Phasen unterschieden, welche auf Guidelines der kardiologischen Rehabilitation basieren [11,12]. Nach der akuten Krankenbehandlung (Phase I) folgt in der Regel ein stationäres Anschlussheilverfahren oder Rehabilitationsheilverfahren statt (Phase II). Das Kosten-Effektivitäts- und Kosten-Nutzen-Verhältnis der Rehabilitation ist richtungweisend für unsere Volkswirtschaft [13-15].

Wissenschaftliche Studien unterstützen die nachhaltige Wirksamkeit einer intensivierten, multimodalen Orthopädischen Rehabilitation (ORehab) mit moderater Evidenz, der subjektive Gesundheitszustand wird verbessert und die Schmerzintensität reduziert [16]. Für die Rehabilitation nach Hüft- und Knie-TEP [17-23] und bei chronischem Rückenschmerz [24-29] wird der Evidenzlevel Ia/Ib angegeben.

Die Bedeutung der Rehabilitation und Prävention wird in Zukunft weiter zunehmen [30]

Situation in Österreich

In Österreich stellt das Gesundheitsqualitätsgesetz (GQG) die Grundlage für eine bundesweite Sicherung der Qualität im Gesundheitswesen dar. Neben den Austrian Inpatient Quality Indicators (A-IQI) und dem Österreichisches Gesundheitsinformationssystem (ÖGIS) gibt es Qualitätsregister für ausgewählte medizinische Bereiche. Aus Routinedaten werden statistische Auffälligkeiten für definierte Krankheitsbilder in einzelnen Krankenanstalten identifiziert. Betrachtet werden dabei in erster Linie Sterbehäufigkeiten, aber auch Operationstechniken, Komplikationen, Mengeninformationen, sowie Versorgungs- und Prozessindikatoren. Es werden Qualitätsberichte und Health Technology Assessments (HTA) erstellt [31]. Die Rehabilitationseinrichtungen haben dabei die Voraussetzungen für interne Maßnahmen der Qualitätssicherung zu schaffen.

Bei Erkrankungen des Stütz- und Bewegungsapparates durch entzündliche und degenerative Erkrankungen, Verletzungsfolgen oder nach operativen Eingriffen, kann eine dreiwöchige stationäre Orthopädische Rehabilitation (ORehab; WHO - Phase II [11,12]) zur Wiederherstellung der Gesundheit und Reintegration in das soziale und berufliche Umfeld in Anspruch genommen werden.

Nach einer dreijährigen Pilotphase der Pensionsversicherungsanstalt [32] besteht seit 2018 flächendeckend die Möglichkeit einer aktiven Gesundheitsvorsorge mit medizinisch-sekundärpräventivem Fokus, welche die klassische dreiwöchige Kur in Österreich ersetzen soll. Der modulare Aufbau der Gesundheitsvorsorge Aktiv (GVA) mit den bedarfsorientierten Schwerpunkten Bewegung (Motivation und Optimierung) und Mentale Gesundheit zeichnet sich durch einen erhöhten Anteil aktiver Therapieformen aus. Der Unterschied der beiden stationären Angebote liegt im präventiven Charakter der GVA. In der GVA ist das Patientengut im Vergleich zur ORehab in der Regel jünger und es sind noch keine manifesten Erkrankungen des Stütz- und Bewegungsapparates eingetreten, die spezieller Rehabilitationsmaßnahmen bedürfen würden. Neben einer ähnlichen ICD-Klassifikation degenerativer, entzündlicher muskuloskelettaler Beschwerden (vgl. Tab.1) sind Funktionsfähigkeit und Gesundheit bei GVA-Patienten ebenso wie bei orthopädischen Patienten eingeschränkt. Es liegt jedoch kein rezenter operativer Eingriff am Stütz- und Bewegungsapparat vor (vgl. WHO - Phase I; Akutereignis, -versorgung).

In Rahmenverträgen mit dem Hauptverband der Österreichischen Sozialversicherungsträger, insbesondere der Pensionsversicherungsanstalt, gibt es klare Leistungsvereinbarungen für die ORehab und die GVA [vgl. Evidenzbasierte Therapiemodule der Deutschen Rentenversicherung: 23]. Neben Strukturqualitätskriterien (Ausstattung und Leistungsangebot) sind Aspekte der Prozess- und Ergebnisqualität klar definiert [11]. Dazu zählen Ergebnisanalysen, welche eine standardisierte Erfassung von Outcome-Parametern, bei Beginn und Ende des Rehabilitationsaufenthaltes, zur Dokumentation des Rehabilitationserfolges im Entlassungsbericht vorsehen. Auswertungen oder Veröffentlichungen dieser medizinischen Routinedaten in Fachzeitschriften sind jedoch nur anhand einzelner Pilotprojekte oder für spezifische Fragestellungen verfügbar.

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Medizinische Ergebnisqualität

Medizinische Ergebnisqualität ist die *„messbare Veränderung des professionell eingeschätzten Gesundheitszustandes, der Lebensqualität und der Zufriedenheit eines Patienten"* [vgl. GQG] und wird sichtbar gemacht durch *„die Differenz zwischen dem Eingangszustand und dem Ausgangszustand"* [vgl. Donabedian, 33].

Die Ergebnismessung kann in der Rehabilitation auf verschiedenen methodischen Zugängen basieren, wie Fragebögen, Leistungstests, apparativen Messungen und ärztlichen Körperfunktionsuntersuchungen [34]. Die Ergebnisqualität, der „Outcome", umfasst Merkmale auf gesundheitlicher (z.B. Symptome, Schmerz), funktionaler (z.B. Leistung) und edukativer Ebene [35]. Neben der subjektiven Einschätzung durch den Patienten („Patient-Reported Outcomes (PRO)" [36]) erfolgt eine Dokumentation von diagnostischen, medizinischen Parameter und weiteren relevanten Zielgrößen/-kriterien (z.B. ICF) durch das medizinische Fachpersonal.

Ziel der vorliegenden Arbeit ist es, auf Basis der routinemäßigen Datenerfassung (Routine Outcome Measurement) eine valide Bewertungsgrundlage der medizinischen Ergebnisqualität bereitzustellen. Dabei stehen allgemeine (unspezifische, konstitutionelle) und nicht indikationsspezifische Kennwerte im Mittelpunkt. Kontinuierlich erfasste medizinische Referenzwerte haben einen vielfältigen potentiellen Nutzen in Bereichen der Qualitätssicherung, Bewusstseinsbildung, für Zielvereinbarungen und als Entscheidungsgrundlage zur Evaluation unterschiedlicher Versorgungsmodelle.

Material und Methodik

Die im Leistungsprofil der österreichischen Sozialversicherungsträger geforderten medizinischen Outcome-Parameter der Ergebnisqualität bzw. deren Änderungen bilden die Grundlage der vorliegenden Arbeit, welche standardisierte Kennzahlen des Rehabilitationserfolgs deskriptiv aufbereitet und unspezifische monozentrische Referenzdaten für die ORehab und GVA bereitstellt. Die Datenerhebung erfolgte von Ärzten und medizinischem Fachpersonal im Routinebetrieb. Standardisierte klinische Kennwerte der Patienten werden systematisch zu Aufnahme- und Entlassungszeitpunkt numerisch erfasst und in einem EDV-System archiviert. Die einfach quantifizierbaren, numerischen Outcome-Parameter der Ergebnisqualität beinhalten allgemeine Gesundheitsmerkmale, wie Körpermaße und Kreislaufparameter, psychologische Indikatoren wie Schmerz und subjektiven Gesundheitszustand (vgl. Abb.1). Diese unspezifischen Kennwerte der Ergebnisqualität sind bei allen Indikationen zu Beginn und Ende der Phase II Rehabilitation im Entlassungsbericht zu dokumentieren (Prä-Post-Vergleich) bzw. werden inhaltlich und faktoranalytisch in einem einfachen deskriptiven Evaluationsmodell zu drei unabhängigen Faktoren bzw. einem Gesamtwert zusammengefasst (vgl. Abb.1 & Tab.2).

Für Knie- und Hüft-TEP Patienten in der ORehab ergibt sich aus den unterschiedlichen Antrittszeiten [Zeitraum zwischen Akutversorgung (OP-Zeitpunkt) und dem Beginn des Anschlussheilverfahrens (AHV)] eine quasiexperimentelle Kontrollgruppe (Wartegruppe).

Klinische Referenzstichprobe am Prüfzentrum

Im Leistungszeitraum 2016 - 2018 wurden insgesamt 11.414 Patienten am Humanomed Zentrum Althofen in den Indikationen ORehab & GVA erfasst (54,7 +/- 12,3 Jahre; 52,9% Frauen). Lebensalter und Geschlechterverhältnis sind zwischen den beiden

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Gesundheitsprogrammen unterschiedlich. Der Frauenanteil ist in der GVA etwas höher (54,7% vs. 51,1%), die Altersdifferenz zwischen den Indikationen beträgt 12,6 Jahre. Die Mehrzahl der GVA-Patienten ist zwischen 41 und 50 Jahren alt. Das Durchschnittsalter der ORehab liegt hingegen knapp über 60 Lebensjahren (vgl. Tab.1). Eine Kategorisierung der muskuloskelettalen Erkrankung (M) oder Verletzung (S) erfolgte anhand der Einweisungsdiagnose nach ICD-10. Die Mehrzahl der Patienten kommt auf Grund von Rückenbeschwerden zur Rehabilitation (59,1%). Der Anteil der Wirbelsäulen-/Rückenpatienten liegt in der GVA bei 88,6%. In der ORehab sind es 31,4%, gefolgt von Gelenkserkrankungen der oberen/unteren Extremitäten, wie Knie (21,7%), Hüfte (15,6%) und Schulter (7,2%). Patienten mit operativen Eingriffen (OP) befinden sich ausschließlich in der ORehab-Stichprobe. Von diesen wurden 31,5% mit einer Endoprothese (EP) versorgt. Der Anteil der EP-Versorgungen lag bei den Kniepatienten bei 64,1%, bei Hüftpatienten bei 85,0% und bei peripheren Gelenken bei 35,9%.

Tabelle 1: Analysestichprobe im Leistungszeitraum 2016-2018.

Klassifikation nach ICD-10 Lokalisation/Hauptdiagnose	HZA-Indikation		Gesamt	Alter (MW +/- SD)		Frauenanteil	
	GVA	ORehab		GVA	ORehab	GVA	ORehab
Rücken	4895	1850	6745	48,0	57,0	2706	913
M41, M43, M48, M50, M51, M53, M54, S32, S22, S12	88,6%	31,4%	59,1%	5,5	13,2	55,3%	49,4%
Knie	170	1277	1447	49,2	63,8	73	702
M17, M23, S83	3,1%	21,7%	12,7%	5,0	13,0	42,9%	55,0%
Hüfte	64	916	980	49,7	67,1	29	487
M16	1,2%	15,6%	8,6%	4,6	11,2	45,3%	53,2%
Schulter	103	719	822	49,2	58,0	56	326
M75, S42, S43, S46	1,9%	12,2%	7,2%	5,4	11,1	54,4%	45,3%
Unter-/Oberschenkel	1	416	417	0,0	61,1	0,0	230
S82, S86, S72	0,0%	7,1%	3,7%	0,0%	16,3	0,0%	55,3%
sonstige Arthrose	184	234	418	48,5	62,4	90	134
M19, M25	3,3%	4,0%	3,7%	5,6	13,6	48,9%	57,3%
sonstige (Komplik. EP, Unterarm, Weichteile, Enthesopathien, Nekrose, Fußfraktur, Polyarthritis	55	202	257	47,8	60,4	35	99
T84, S52, M79, M77, M87, S92, M06	1,0%	3,4%	2,3%	6,0	14,4	63,6%	49,0%
weitere Erkrankungen (Stütz-/Bewegungsapp.)	54	274	328	47,5	54,8	33	127
ICD-10Kat < **n=20**	1,0%	4,7%	2,9%	5,7	15,1	61,1%	46,4%
Gesamt *Indikationsunterschiede:*	**5526**	**5888**	**11414**	**48,1**	**60,7**	**3022**	**3018**
Alter: p=.000 (t-Test), Geschlecht:p=.000 (CHI²)	100,0%	100,0%	100,0%	**5,5**	**13,6**	**54,7%**	**51,3%**
N=11.414 mit mehr als 18 Aufenthaltstagen	**GVA**	**ORehab**	**Gesamt**	**MW**	**SD**	**Anzahl**	**%**
	48,4%	**51,6%**	**11414**	**54,7**	**12,3**	**6040**	**52,9%**

Die durchschnittliche Aufenthaltsdauer in ORehab und GVA betrug 21,88 +/- 2,3 Tage (ORehab: 21,98 +/- 2,7; GVA: 21,75 +/- 1,8 Tage). 2,1 Prozent aller Patienten brachen ihre stationäre Behandlung aufgrund eines Verlustes der Rehabilitationsfähigkeit (z.B. akute Erkrankung) oder privater Gründe vorzeitig ab (Kriterium<=18 Verpflegungs-tage). Abbrecher zeigten zum Aufnahmezeitpunkt einen leicht erhöhten Ruhepuls (80,5 +/- 12,1 bpm) und einen etwas schlechteren subjektiven Gesundheitszustand (EQ-VAS: 58,2 +/- 18,4; vgl. Tab.3). Weitere klinische Basisdaten weisen keine signifikanten Unterschiede zwischen Patienten mit <=18 vs. >19 Verpflegungstagen, der

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multivariate Effekt ist gering (partielles Eta^2=.004). Bei 1,9% der Rehabilitanden betrug der stationäre Aufenthalt vier Wochen (nur in der ORehab; $Anteil_{ORehab}$: 3,5%).
Der Zeitraum zwischen Akutversorgung (OP) betrug in der ORehab im Mittel 8,4 +/- 4,1 Wochen, wobei Knie- und Hüft- TEP-Patienten früher von Phase I in die Phase II kommen (Median: sechs Wochen)[1].

Ethische Aspekte

Personen- und gesundheitsbezogene Daten werden im Rahmen der routinemäßigen medizinischen Versorgung und des Qualitätsmanagements am Humanomed Zentrum Althofen (9330 Althofen, Moorweg 30) standardisiert erfasst (Verantwortlich für die gegenständliche Datenverarbeitung: Humanomed Zentrum Althofen GmbH; Datenschutzbeauftragter: Mag. Karl Klein, Jesserniggstraße 9, 9020 Klagenfurt).
Die der Veröffentlichung zu Grunde liegenden Datensätze aus dem Krankenhaus-Informations-System wurden unter Einhaltung aller Vorschriften der DSGVO, des DSG und der Deklaration von Helsinki in der jeweils aktuellen Fassung, auf Basis nationaler Rechtsgrundlagen (KAKuG, Verträge mit Sozialversicherungsträgern etc.) im überwiegend öffentlichen Interesse wissenschaftlich dokumentiert.

Quantifizierung der unspezifischen „Medizinischen Ergebnisqualität"

Neben der deskriptiven Aufbereitung einzelner Kennwerte werden Effekte des stationären Rehabilitationsaufenthalts, die „unspezifische" Medizinische Ergebnisqualität (MEQ), anhand repräsentativer monozentrischer Normdaten berechnet (N_{2016-}

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[1] Der Beginn des AHV erfolgt am Prüfzentrum später als z.B. in Deutschland (innerhalb von 14 Tagen nach Entlassung). In Österreich kann ein AHV drei bis vier Monate ab Bewilligungsdatum in Anspruch genommen werden. Für ein (R)HV [(Rehabilitations-)Heilverfahren] beträgt die zeitliche Befristung acht bis 12 Monate, der Antritt der GVA muss innerhalb neun Monate ab Antragsbewilligung erfolgen.

18=11.414; vgl. Tab.1). Dabei wird ein Gesundheitszustandsindex durch faktorenanalytische Zusammenfassung der obligatorisch zu erfassenden klinischen Basisdaten der Patienten (vgl. Tab.2) berechnet. Er entspricht dem arithmetischen Mittel dreier unabhängiger Bereiche (vgl. Abb.1): Körpermaße (BMI und Bauchumfang), Kreislaufparameter (Blutdruck und Ruhepuls) und Beschwerden (visuelle Analogskalen [VAS-Schmerz, 37] und subjektiver Gesundheitszustand [EQ-VAS, 38]) und soll einen einfachen und schnellen Überblick zur „unspezifischen" Wirksamkeit eines rehabilitativen Aufenthalts vermitteln. Der Gesundheitszustandsindex kann als Indikator des allgemeinen Gesundheitszustands bzw. der aktuellen konstitutionellen Verfassung interpretiert werden.

Die Auswahl der klinischen Parameter folgt den Anforderungen im Leistungsprofil der österreichischen Sozialversicherungsträger zur Ergebnisanalyse, welche einen vergleichbaren medizinischen Qualitätsstandard garantieren sollen.

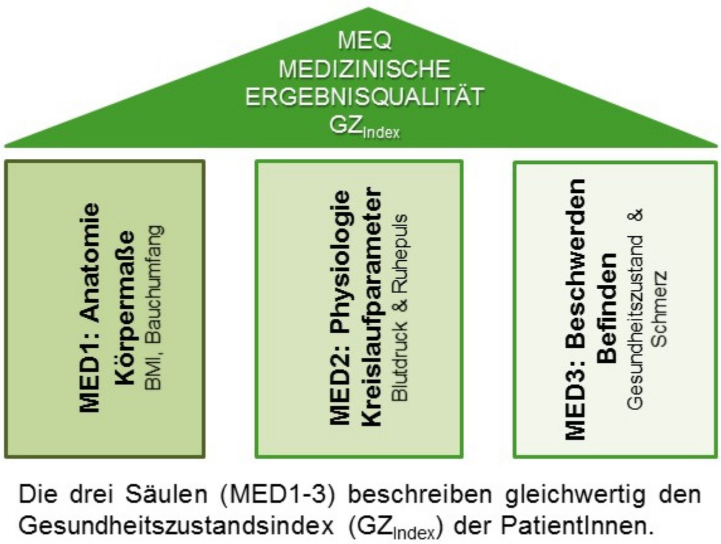

Abbildung 1: Evaluationsmodell - allgemeine Faktoren der unspezifischen Medizinischen Ergebnisqualität.

Für die Berechnung der drei Faktoren (MED_{1-3}) und Gesamtwert (GZi) vgl. Tabelle 2.

Auf Basis der Werteverteilungen werden die einzelnen Outcome-Parameter in z-Werte transformiert, welche eine Umrechnung in Perzentile ermöglichen. Anhand der z-Normierung können unterschiedlich skalierte Messgrößen zusammengefasst und Veränderungen einheitlich quantifiziert werden. Ein Wert von 50% (Median) bzw. ein z-Wert von Null entspricht - bei gegebener Normalverteilung - dem repräsentativen Mittelwert von Aufnahme- und Entlassungsdaten aller Patienten am Prüfzentrum. Unterschiede von Aufnahme zu Entlassung, werden mit Hilfe von Effektstärken [39] und anhand jener Patientenanzahl (relativer Häufigkeiten) veranschaulicht, welche sich klinisch relevant verbessern konnten (kategoriale Darstellung: besser, gleich, schlechter). Als Schwellenwert kommt eine mittlere z-Differenz >0,20 (MED1-3) bzw. >0,33 (Gesundheitszustandsindex) zur Anwendung [40,41]. Alternativ dazu wird die durchschnittliche (Perzentil-)Veränderung im Vergleich zum Aufnahmezeitpunkt berechnet und ggf. indikationsspezifisch aufbereitet.

Die statistische Datenverarbeitung erfolgte mit IBM® SPSS® Statistics (Version 22). Bei der statistischen Analyse kamen neben deskriptiven Methoden parametrische Verfahren wie mehrfaktorielle Varianzanalysen für Messwiederholungen [(M)AN(C)OVA; Zwischensubjekteffekte: Indikation (2), Geschlecht (2), Kovariate: Alter, Innersubjekteffekt: Rehabverlauf (2)], Regressionen und Pearson Korrelationen zum Einsatz. Einzelne fehlende Werte wurden für die statistische Analyse nicht ersetzt. Auf die Angabe von p-Werten wird verzichtet, stattdessen kommen vorzugsweise Effektstärken [part. Eta^2 und standardisierte Mittelwertdifferenzen (Cohen's d bzw. z-Werte/-Differenzen) zum Einsatz. Die Darstellung des partiellen Eta^2 (η^2) wurde gewählt, da bei der vorliegenden Stichprobengröße bereits sehr geringe numerische Unterschiede statistisch signifikant werden, auch wenn diese inhaltlich und klinisch nicht relevant sind. Ein η^2

zwischen .01-.06 entspricht einem kleinen Effekt, Ausprägungen von .06-.14 einem mittleren Effekt und Werte >.14 einem großen Effekt [42]. Die Anwendung multivariater Varianzanalysen (MANOVA) und eine faktorenanalytische Reduktion der klinischen Basisdaten zu drei Faktoren bzw. einem Gesamtwert (Gesundheitszustandsindex) folgt inhaltlichen, statistischen Überlegungen und zur besseren Übersichtlichkeit.

Ergebnisse

Die im Ergebnisteil vorgestellten monozentrischen klinischen Referenzdaten basieren auf Patienten mit Beschwerden des Stütz- und Bewegungsapparates, die eine dreiwöchige stationäre ORehab oder GVA absolvierten. Die im medizinischen Leistungsprofil geforderten anatomischen, physiologischen und psychologischen Outcome-Parameter der unspezifischen Ergebnisqualität (MEQ; vgl. Abb.1) werden faktoren- bzw. regressionsanalytisch, ohne gravierenden Informationsverlust (Varianzaufklärung 71%) zu drei Faktoren zusammengefasst (vgl. Tab.2). Die drei Faktoren „Körpermaße" (MED1), „Kreislaufparameter" (MED2) und „Beschwerden" (MED3) bilden zu gleichen Teilen einen „Gesundheits-Zustands-Index" (GZ_{Index})[2]. Für eine Gesamtbewertung der MEQ werden die Veränderung von Aufnahme zu Entlassung in den Faktoren herangezogen.

[2] Wenn man die Werte eines „gesunden" Menschen in die Regressionsgleichungen in Tab. 2 zur Berechnung der MEQ-Faktoren eingibt, erhält man negative Ausprägungen in den MEQ-Faktoren mit einem zu erwartenden GZi kleiner minus 0,5.

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Tabelle 2: Faktorenbildung der unspezifischen MEQ.

Hauptkomponentenanalyse - Eichstichprobe: ORehab vs. GVA

Faktor	Kennwert	Kommunalität	Faktorladung (rotiert)	% der Varianz	Beta-Koeffizient	Regressionsgleichung
FAKTORENANALYSE (PCA, Varimax) mit Aufnahme- und Entlassungsdaten (N=22.789 Messungen)						
MED 1 [z]: Anatomische Merkmale	**BMI** [kg/m²]	0,933	0,958	**33,2340**	0,520	MED1= -6.583 + BMI * 0.100 + Bauchumf. * 0.038
	Bauchumfang [cm]	0,934	0,955		0,503	R=0,989
MED 2 [z]: Kreislauf Merkmale	**RRsys** [mmHG]	0,725	0,855	**20,5020**	0,558	MED2= -12.833 + RRdia * 0.075 + RRsys * 0.042 + RP * 0.022
	RRdia [mmHG]	0,740	0,824		0,480	
	Ruhepuls (RP) [bpm]	0,162	0,395		0,255	R=0,986
MED 3 [z]: Beschwerden	**VAS** [cm; 0-10]	0,731	0,852	**17,0890**	0,583	MED3= 1.555 + VAS * 0.269 + GSZS * -0.034 .
	GSZS [%; 0-100]	0,732	-0,851		-0,581	R=0,996
Gesundheitszustandsindex GZi		**Mittelwert aus MED1, MED2 und MED3**			3 Faktoren	**70,83% Varianzaufklärung**

RRsys/dia … systolischer/diastolischer Blutdruck; RP … Ruhepuls; VAS … Visuelle Analog Skala (Schmerz; 0-10); GSZS … Gesundheitszustand (0-100; EQ-VAS); Hohe (positive) Werte [z] entsprechen einem ungünstigeren Wert.

PCA (Varimax Rotation): 71% Varianzaufklärung; MED1: 33%, MED2: 21%, MED3: 17%. Die allgemeinen Outcome-Parameter bzw. drei Faktoren zu einem Mittelwert zusammenfasst ergeben den „Gesundheitszustandsindex (GZIndex)". Es gibt keine Mehrfachladungen (>.20), die Faktorenstruktur ist stabil.

Die zeitliche Stabilität bzw. Korrelation (r) der MEQ-Faktoren zwischen Rehabilitationsbeginn und Rehabilitationsende liegt bei: r=.989 (MED1), r=.301 (MED2), r=.654 (MED3) und r=.723 für den GZIndex (vgl. Tab.3).

Ausgangswerte zu Rehabilitationsbeginn

Die medizinischen Ausgangswerte (AGW) zu Rehabilitationsbeginn sind auf Grund der Zuweisungsbestimmungen von der Indikation abhängig (GVA vs. ORehab), welche soziodemografische Unterschiede in Alter, Geschlecht und Beschwerdebild (Zwischensubjektfaktoren; vgl. klinische Referenzstichprobe, Tab.1) aufweist.

Der multivariate AGW-Unterschied zwischen den Indikationen (MANCOVA: part. Eta^2 [η^2]=.118 / .028) bei den Einzelwerten (/Faktoren) wird maßgeblich vom Geschlecht (η^2=.207 / .072; Zwischensubjekteffekt) und vom Lebensalter (η^2=.070 / .010; Kovariate) beeinflusst, die einen wesentlichen Beitrag zu den beobachtbaren AGW liefern (alters-/geschlechtsbereinigter Indikationseffekt: η^2=.069 / .016)[3]. Das Geschlecht hat, neben Merkmalen wie der Körpergröße (nicht im Modell berücksichtigt), v.a. Einfluss auf Bauchumfang (η^2=.076) und systolischen Blutdruck (η^2=.045), beide Kennwerte sind bei Frauen deutlich geringer (vgl. auch MED1, MED2 in Tab.6a).

Abhängigkeiten der medizinischen Kennwerte mit dem Lebensalter zeigen, dass v.a. ältere Rehabilitanden einen höheren systolischen Blutdruck aufweisen (r=.165), welcher mit einem größeren BMI (r=.293) und Bauchumfang (r=.320) in Beziehung steht. Der Einfluss des Lebensalters und des Geschlechts auf das multivariate Rehabilitationsergebnis (Differenzwerte) ist jedoch relativ gering ausgeprägt (η_{Alter}^2=.017 [alle Einzelkorrelationen: r<.100]; $\eta_{Geschlecht}^2$=.025; vgl. Fußnote 3).

[3] Der moderierende Einfluss der Gruppierungsmerkmale (Haupteffekte) auf die AGW (vgl. auch Tab.6a) ist in ähnlicher Größenordnung auch im statistischen Gesamtmodell mit Aufnahme- und Entlassungsdaten zu beobachten, wobei diese nicht maßgeblich für das Ausmaß der beobachteten Veränderungen (Wechselwirkungen) sind (vgl. Tab.3, Tab.4 und Tab.6b).

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Tabelle 3: Ausgangswerte GVA vs. ORehab und unspezifische MEQ.

MEQ Indikatoren & Faktoren		Indikationsunterschiede: Aufnahme (AGW)					Änderung: Rehabbeginn (prä) zu Rehabende (post)					
Outcome-Kennwert		N	Mittelwert +/- Standardabweichung		Differenz (GVA-ORehab)	part. Eta² (ohne Kov.)	mittlere Diff. (post - prä) +/- SD		(z) normierte Differenz +/-SD		Korrelation Prä-Post	part. Eta² (ohne Kov.)
BMI [kg/m²]	GVA	5508	27,98	5,23	-0,94	0,008	-0,35	0,72	-0,07	0,14	0,99	0,189
	ORehab	5788	28,92	5,32			-0,21	0,85	-0,04	0,16	0,99	0,057
	Gesamt	**11296**	**28,46**	**5,30**			**-0,28**	**0,79**	**-0,05**	**0,15**	**0,99**	**0,109**
Bauchumfang [cm]	GVA	5466	97,25	13,13	-3,16	0,014	-1,56	1,89	-0,12	0,14	0,99	0,405
	ORehab	5808	100,41	13,47			-0,98	2,08	-0,07	0,16	0,99	0,183
	Gesamt	**11274**	**98,88**	**13,40**			**-1,26**	**2,01**	**-0,10**	**0,15**	**0,99**	**0,284**
MED 1: Anatomische Merkmale [z]	GVA	5448	-0,09	0,99	-0,21	0,011	0,09	0,13	0,09	0,13	0,99	0,344
	ORehab	5715	0,13	1,01			0,06	0,13	0,06	0,13	0,99	0,161
	Gesamt	**11163**	**0,02**	**1,01**			**0,08**	**0,13**	**0,08**	**0,13**	**0,99**	**0,246**
RRsys [mmHG] (systolischer Blutdruck)	GVA	5525	128,88	12,71	-2,61	0,012	-4,76	13,38	-0,42	1,17	0,33	0,110
	ORehab	5885	131,49	11,33			-5,28	12,94	-0,46	1,14	0,26	0,144
	Gesamt	**11410**	**130,23**	**12,09**			**-5,03**	**13,15**	**-0,44**	**1,15**	**0,30**	**0,127**
RRdia [mmHG] (diastolischer Blutdruck)	GVA	5525	77,48	8,03	0,37	0,001	-1,94	9,81	-0,26	1,32	0,18	0,037
	ORehab	5883	77,11	7,45			-2,33	9,21	-0,31	1,24	0,13	0,060
	Gesamt	**11408**	**77,29**	**7,74**			**-2,14**	**9,51**	**-0,29**	**1,28**	**0,16**	**0,048**
Ruhepuls [bpm]	GVA	5523	78,59	11,87	-0,21	0,000	-1,38	12,54	-0,12	1,09	0,42	0,012
	ORehab	5870	78,80	11,69			-1,58	12,10	-0,14	1,05	0,43	0,016
	Gesamt	**11393**	**78,70**	**11,77**			**-1,48**	**12,31**	**-0,13**	**1,07**	**0,43**	**0,014**
MED 2: Kreislauf Merkmale [z]	GVA	5522	0,12	1,11	-0,09	0,002	0,38	1,19	0,38	1,19	0,32	0,090
	ORehab	5867	0,21	0,98			0,43	1,09	0,43	1,09	0,28	0,134
	Gesamt	**11389**	**0,16**	**1,04**			**0,40**	**1,14**	**0,40**	**1,14**	**0,30**	**0,111**
VAS [cm; 0-10] (Schmerz)	GVA	5526	4,81	1,87	1,11	0,070	-2,09	1,56	-0,97	0,72	0,64	0,644
	ORehab	5880	3,70	2,12			-1,65	1,66	-0,76	0,77	0,65	0,498
	Gesamt	**11406**	**4,24**	**2,08**			**-1,87**	**1,63**	**-0,86**	**0,75**	**0,66**	**0,569**
GSZS [%; 0-100] (Gesundheitszustand; EQ5D)	GVA	5522	66,26	17,30	2,27	0,005	13,91	13,06	0,81	0,76	0,66	0,533
	ORehab	5884	63,99	16,70			13,79	14,91	0,81	0,87	0,56	0,461
	Gesamt	**11406**	**65,09**	**17,03**			**13,85**	**14,05**	**0,81**	**0,82**	**0,61**	**0,494**
MED 3: Beschwerden [z]	GVA	5522	0,60	0,87	0,22	0,015	1,04	0,69	1,04	0,69	0,66	0,696
	ORehab	5876	0,37	0,93			0,91	0,76	0,91	0,76	0,65	0,595
	Gesamt	**11398**	**0,48**	**0,91**			**0,97**	**0,73**	**0,97**	**0,73**	**0,65**	**0,644**
GZi: Gesundheits-zustandsindex [z]	GVA	5441	0,21	0,66	-0,03	0,000	0,50	0,47	0,50	0,47	0,72	0,534
	ORehab	5689	0,24	0,61			0,47	0,45	0,47	0,45	0,72	0,523
	Gesamt	**11130**	**0,22**	**0,64**			**0,48**	**0,46**	**0,48**	**0,46**	**0,72**	**0,528**

Zum Aufnahmezeitpunkt in die Rehabilitation beträgt der durchschnittliche BMI 28,5 +/- 5,3 Einheiten (34,1% der Patienten haben einen BMI>30), der Bauchumfang liegt bei 98,9 +/- 13,4 cm, wobei zwischen den Indikationen ein moderater Unterschied in den anatomischen AGW (MED1; $z_{Differenz}$=-0,21, η^2=.011) besteht.

Der mittlere Blutdruck bei Aufnahme beträgt 130,2 +/- 12,1 zu 77,3 +/- 7,7 mmHG (52,1% der Patienten sind hyperton), der AGW-Ruhepuls liegt bei 78,7 +/- 11,8 bpm (vgl. Tab.3). Ein Indikationsunterschied in Kreislaufmerkmalen (MED2) ist vorhanden, aber im Mittel relativ gering ausgeprägt ($z_{Differenz}$=-0,09; η^2=.002) bzw. schwindet dieser Indikationseffekt, wenn man Geschlecht und Alter in den beiden Substichproben berücksichtigt.

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Im Gegensatz dazu zeigt sich in den Beschwerden (MED3) der deutlichste Unterschied ($z_{Differenz}$=0,22; η^2=.015) zwischen GVA und ORehab. Die wahrgenommenen Schmerzen (VAS; 0-10) der Patienten liegen bei 4,3 +/- 2,1 und sind in der GVA (4,8 vs. 3,7 in ORehab) und allgemein bei jüngeren Patienten ($r_{VAS\text{-}Alter}$=-.134) stärker ausgeprägt. Der AGW im subjektiven Gesundheitszustand (EQ-VAS; 0-100) wird in der ORehab deskriptiv etwas kritischer eingeschätzt (64,0% vs. 66,3% in der GVA).

Veränderung von Aufnahme zu Entlassung

Der Effekt des Rehabilitationsaufenthalts, die Änderung zwischen Ausgangs- und Entlassungszustand, ist zwischen den beiden Indikationen ähnlich stark ausgeprägt (vgl. Tab.3-6). GVA Patienten verbessern sich im Vergleich zur orthopädischen Rehabilitanden deutlicher in anatomischen Merkmalen (MED1) und Beschwerden (MED3), wohingegen in der ORehab Verbesserungen in kreislaufbezogenen Merkmalen (MED2) deskriptiv etwas besser ausfallen (Tab.3 & 5).

In der statistischen multivariaten Gesamtbewertung (vgl. Tab.4a) mit Aufnahme- und Entlassungsdaten zeigt sich die deutliche Änderung in der unspezifischen MEQ ($\eta^2_{unifaktoriell}$=.681; $\eta^2_{multifaktoriell}$=.064), wobei die erfassten Einflussgrößen (Indikation, Geschlecht und Alter) eine vergleichsweise geringere Rolle für die MEQ spielen (vgl. Wechselwirkungen: alle η^2<.03)[4].

Anhand der ORehab-Teilstichprobe der Knie- und Hüft-TEP-Patienten ist zu erkennen (Tab.4b), dass die Veränderungen in der unspezifischen MEQ (η^2=.657) unabhängig

[4] Der Einfluss auf die AGW bzw. Absolutwerte zu Rehabilitationsbeginn ist hingegen merklich (vgl. Tab.6ab), insbesondere des Geschlechts (vgl. Tab.4: HE). Dies spielt jedoch für die Veränderungen (vgl. Tab.4: WW) während des Rehabilitationsaufenthalts eine kleinere Rolle. D.h. im Mittel verändert sich Subgruppen im ähnlichem Ausmaß, unabhängig von ihren AGW.

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vom Rehabilitationseintrittszeitpunkt erfolgen (Wechselwirkung: Zeit x post-OP Woche: η^2=.002). Dieses Ergebnis steht im Kontrast zu (krankheits-)spezifischen Outcome-Kennwerten (WOMAC, Gehtests, ADL) wo dem Eintrittszeitpunkt (post-OP Woche) eine gewichtigere Rolle zukommt (Wechselwirkung: η^2=.029).

Spezifische und unspezifische Ergebnisqualität zeigen dabei eine vergleichbare Änderungssensitivität ($\eta^2_{spezifisch}$=.668 vs. $\eta^2_{unspezifisch}$=.657). Der Zusammenhang zwischen spezifischen und unspezifischen Outcome-Kennwerten(-veränderungen) ist klein (r<.200), was sich bei mehrdimensionaler Betrachtung der zeitlichen Veränderungen varianzaufklärend niederschlägt ($\eta^2_{unifaktoriell}$ =.755).

Tabelle 4a: Statistische Kennwerte zu Rehabilitationseffekten (MEQ).

MANCOVA [(2x)2x2] mit Messwiederholung		**ORehab & GVA - Effektstärken** *(part. Eta²)*			
		MEQ-Einzelwerte*		***MEQ-Faktoren*****	
		HE	**WW: Zeit x UV**	**HE**	**WW: Zeit x UV**
Zeit (2)	**unifakt. Rehab-Effekt**	0,691	-	0,681	-
Zeit [(2)]	**nultifakt. Rehab-Effekt**	0,069	(Kov. Alter: 54,5 J.)	0,064	(Kov. Alter: 54,5 J.)
UV1 [2]	**Indikation**	0,076	0,028	0,012	0,017
UV2 [2]	**Geschlecht**	0,229	0,025	0,075	0,019
Kovariate	**Alter**	0,090	0,004	0,012	0,002

VAS);
***. (Unspezifische) MEQ-Faktoren: MED1, MED2, MED3 und GZi [z];*
HE: Haupteffekt; WW: Wechselwirkung; Kov. … Kovariate;

Tabelle 4b: Teilstichprobe ORehab - "spezifische" EQ vs. "unspezifische" MEQ.

MANCOVA [(2x)5x2] mit Messwiederholung		**Knie-/Hüft-TEP - Effektstärken** *(part. Eta²)*			
		spezifische EQ*		***unspezifische MEQ*****	
		HE	**WW: Zeit x UV**	**HE**	**WW: Zeit x UV**
Zeit (2)	**unifakt. Rehab-Effekt**	0,668	-	0,657	-
Zeit [(2)]	**nultifakt. Rehab-Effekt**	0,016	(Kov. Alter: 67,6 J.)	0,035	(Kov. Alter: 67,6 J.)
UV1 [5]	**post-OP Woche**	0,006	**0,029**	0,004	0,002
UV2 [2]	**Geschlecht**	0,056	0,015	0,035	0,018
Kovariate	**Alter**	**0,150**	0,015	0,015	0,007

**. Spezifische Ergebnisqualität (EQ): WOMAC Summenscore [0-240], Gehtests [sec]: Time up/go, 10m Gehtest, Beeinträchtigungen/ADL (EQ5D; Summenmodell) [0-100];*
***. Unspezifische MEQ-Faktoren: MED1, MED2, MED3 und GZi [z];*

Im unspezifischen Gesamtscore - dem „Gesundheitszustandsindex (GZ_{Index})“ - zeigt sich, dass 73,9% der Patienten unmittelbar vom Rehabilitationsaufenthalt profitieren. 20,1% der Patienten bleiben unverändert und 6,0% verschlechtern sich zwischen Rehabilitationsbeginn und -ende (vgl. Tab.5). Die durchschnittliche Verbesserung in allgemeinen Gesundheitsmerkmalen um 14,6 Perzentilpunkte differenzierter aufgeschlüsselt zeigt, dass anatomische Merkmale - wie Body Mass Index und Bauchumfang - in den drei Wochen bei der Mehrzahl (83,9%) unverändert bleiben. Kreislaufbezogene Merkmale hingegen, wie Blutdruck und Ruhepuls, werden durch die stationäre Rehabilitation unmittelbar beeinflusst, es kann eine mittlere Verbesserung um 11,6

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Perzentilpunkte festgestellt werden. Die deutlichsten Effekte der stationären Rehabilitation sind in Beschwerdekennwerten erkennbar, wo nahezu jeder Rehabilitand (88,6%) über eine signifikante Verbesserung berichtet.

Tabelle 5: Allgemeine Ergebnisqualität.

MEQ: Allgemeine Ergebnisqualität - Rehabilitation Stütz-/Bewegungsapparat

[relative Häufigkeit in %]	*AGW**	besser	gleich	schlechter	Ø-Verbesserung**
GVA	0,9%	74,6	19,4	5,9	*GZ_{Index}: +15,00*
ORehab	0,3%	73,2	20,8	6,0	*GZ_{Index}: +14,15*
Gesundheits-zustandsindex (GZi)	0,6%	**73,9**	**20,1**	**6,0**	***GZ_{Index}: +14,56***

**. AGW… Ausgangswert zu Rehabilitationsbeginn: Ein negativer %-Wert entspricht einem unterdurchschnittlichen (schlechteren) Wert in der Gesamtstichprobe. Ein AGW (Perzentil) um Null bedeutet, dass kein Unterschied zur Gesamtstichprobe besteht (hier: Patienten mit muskuloskelettalen Beschwerden; GVA und ORehab-Patienten) bzw. gibt Auskunft zur Abweichung der*
***. Durchschnittliche Perzentilverbesserung von Aufnahme- zu Entlassungszeitpunkt;*

(Schwellenwert für Klassifikation: MED1-3: 0,20 bzw. GZi: 0,33 [z-Diff.])

[%]	*AGW**	besser	gleich	schlechter	Ø-Verbesserung**
GVA	4,4%	18,4	81,1	0,4	*MED1: +2,63*
ORehab	-1,7%	12,0	86,5	1,5	*MED1: +1,48*
Körpermaße (BMI, Bauchumfang)	1,3%	15,2	83,9	0,9	***MED1: +2,04***
GVA	1,9%	55,1	14,5	30,4	*MED2: +10,41*
ORehab	-0,8%	58,0	14,4	27,5	*MED2: +12,78*
Kreislaufparamter (BD, RP)	0,5%	56,6	14,5	28,9	***MED2: +11,63***
GVA	-3,4%	92,7	5,9	1,4	*MED3: +31,79*
ORehab	3,2%	84,8	10,0	5,3	*MED3: +27,82*
Beschwerden (VAS, GSZS)	0,0%	88,6	8,0	3,4	***MED3: +29,75***

BMI… Body Mass Index, BD… Blutdruck, RP… Ruhepuls, VAS… Visuelle Analog Skala (Schmerz), GSZS… Gesundheitszustand (EQ-VAS);

Zusammenfassend kann in beiden Fachbereichen eine größenordnungsmäßig vergleichbare Verbesserung in allgemeinen Outcome-Parametern der Ergebnisqualität beobachtet werden, über zwei Drittel der Rehabilitanden sprechen gut auf den Rehabilitationsaufenthalt an (Tab.5). Der allgemeine Gesundheitszustand wird signifikant

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verbessert, Risikofaktoren für Herz-Kreislauf- und Stoffwechselerkrankungen reduziert.

Für die Bereitstellung von indikations- und geschlechtsspezifischen Referenzwerten am Prüfzentrum werden die Ausgangs-, Entlassungswerte und zu erwartende Änderung für die drei Faktoren bzw. des GZi in Tabelle 6ab dargestellt. Die Regressionsgleichungen zur Berechnung der Faktoren der MEQ sind in Tabelle 2 ersichtlich.

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Klinische MEQ-Referenzwerte nach Indikation und Geschlecht

Tabelle 6a: MEQ-Faktor-Referenzwerte zu Rehabilitationsbeginn (AGW).

Aufnahmewerte (AGW): Stationäre Rehab Stütz-/Bewegungsapparat

z-Werte*		AGW: Mittelwert +/- Standardabweichung		Korrelation (r) mit Lebensalter	AGW: Frauen			AGW: Männer		
					$CI_{15.9\%}$**	Mittelwert	$CI_{84.1\%}$	$CI_{15.9\%}$	Mittelwert	$CI_{84.1\%}$
MED1: Anatomische Merkmale	GVA	-0,09	0,99	0,04	-1,32	-0,28	0,77	-0,74	0,14	1,02
	ORehab	0,13	1,01	0,08	-1,07	-0,02	1,03	-0,66	0,28	1,21
	Gesamt	**0,02**	**1,01**	**0,11**	**-1,20**	**-0,15**	**0,90**	**-0,70**	**0,21**	**1,12**
MED2: Kreislauf Merkmale	GVA	0,12	1,11	0,07	-1,20	-0,10	0,99	-0,68	0,39	1,45
	ORehab	0,21	0,98	0,05	-0,86	0,08	1,03	-0,66	0,33	1,32
	Gesamt	**0,16**	**1,04**	**0,06**	**-1,04**	**-0,01**	**1,02**	**-0,67**	**0,36**	**1,38**
MED3: Beschwerden	GVA	0,60	0,87	0,03	-0,15	0,73	1,61	-0,39	0,44	1,27
	ORehab	0,37	0,93	0,05	-0,44	0,48	1,40	-0,65	0,27	1,20
	Gesamt	**0,48**	**0,91**	**-0,03**	**-0,30**	**0,60**	**1,51**	**-0,53**	**0,35**	**1,24**
Gesundheits-Zustandsindex	GVA	0,21	0,66	0,07	-0,57	0,11	0,80	-0,30	0,32	0,94
	ORehab	0,24	0,61	0,10	-0,44	0,18	0,80	-0,31	0,29	0,90
	Gesamt	**0,22**	**0,64**	**0,08**	**-0,50**	**0,15**	**0,80**	**-0,31**	**0,31**	**0,92**

**. Positivere (z-)Werte entsprechen hier einem schlechteren Wert (AGW) zum Aufnahmezeitpunkt; **. CI … Vertrauensintervall (+/- 1 SD).*

Tabelle 6b: MEQ-Faktor-Referenzwerte zu Rehabilitationsende und Rehaberfolg.

Entlassungs- (E) und Differenzwerte (D): Stationäre Rehab Stütz-/Bewegungsapparat

z-Werte		E: Mittelwert +/- Standardabweichung		D: Differenz* +/- SD		E: Frauen			E: Männer		
						$CI_{15.9\%}$	Mittelwert**	$CI_{84.1\%}$	$CI_{15.9\%}$	Mittelwert	$CI_{84.1\%}$
MED1: Anatomische Merkmale	GVA	-0,19	0,93	-0,09	0,13	-1,35	-0,36	0,63	-0,79	0,02	0,84
	ORehab	0,07	0,97	-0,06	0,13	-1,09	-0,07	0,95	-0,68	0,21	1,09
	Gesamt	**-0,06**	**0,96**	**-0,08**	**0,13**	**-1,23**	**-0,22**	**0,80**	**-0,74**	**0,12**	**0,98**
MED2: Kreislauf Merkmale	GVA	-0,26	0,91	-0,37	1,18	-1,30	-0,40	0,51	-0,99	-0,09	0,81
	ORehab	-0,23	0,83	-0,43	1,09	-1,15	-0,33	0,50	-0,95	-0,12	0,71
	Gesamt	**-0,24**	**0,87**	**-0,40**	**1,14**	**-1,23**	**-0,36**	**0,50**	**-0,97**	**-0,11**	**0,76**
MED3: Beschwerden	GVA	-0,44	0,79	-1,04	0,69	-1,19	-0,36	0,46	-1,27	-0,54	0,20
	ORehab	-0,53	0,86	-0,91	0,75	-1,34	-0,48	0,38	-1,45	-0,59	0,28
	Gesamt	**-0,49**	**0,83**	**-0,97**	**0,72**	**-1,27**	**-0,42**	**0,42**	**-1,37**	**-0,56**	**0,24**
Gesundheits-Zustandsindex	GVA	-0,29	0,58	-0,50	0,47	-0,99	-0,37	0,24	-0,73	-0,20	0,33
	ORehab	-0,23	0,56	-0,47	0,45	-0,87	-0,29	0,28	-0,71	-0,17	0,38
	Gesamt	**-0,26**	**0,57**	**-0,48**	**0,46**	**-0,93**	**-0,33**	**0,26**	**-0,72**	**-0,18**	**0,35**

**. Negative (z-Differenz-)Werte entsprechen hier einer Verbesserung von Aufnahme zu Entlassung; **. Absolutwerte (z) - negativere Werte entsprechen einer stärkeren Verbesserung; SD … Standardabweichung.*

Anmerkung: Die Korrelationen der MEQ-Faktoren mit dem Alter sind stabil bzw. sind diese bei Aufnahme- und Entlassungswerten identisch (nicht dargestellt). Der Zusammenhang des Lebensalters mit den Differenzwerten geht gegen Null. Die individuellen Ausgangswerte (AGW) zeigen den zu erwartenden Zusammenhang mit den Differenzwerten (D; E – AGW) in einer Größenordnung von $r_{GZI\ (AGW\ vs.\ E-AGW)}$=-.489. D.h. schlechtere Ausgangswerte zu Rehabilitationsbeginn gehen im Einzelfall mit einer stärkeren Veränderung (Verbesserung) einher.

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Diskussion

Medizinisch-sekundärpräventive Programme sind Gegenstand laufender, teilweise kontrovers geführter Diskussionen. Eine ökonomische, standardisierte Verwertung von allgemeinen medizinischen Outcome-Parametern ist noch die Ausnahme.

Rehabilitationseinrichtungen haben bereits jetzt die Voraussetzungen für interne Maßnahmen der Qualitätssicherung zu schaffen. Hier findet das medizinische Gestalten und Handeln statt, mit dem Ziel einer patientengerechten Versorgung unter Berücksichtigung wirtschaftlicher Komponenten und Vorgaben der Kostenträger.

Auf Basis einer kontinuierlichen Datenerfassung liefert die vorliegende Arbeit eine valide Bewertungsgrundlage der medizinischen Ergebnisqualität für Organisationen, Behandler und Patienten. Dabei stehen allgemeine unspezifische und nicht indikationsspezifische Kennwerte im Mittelpunkt, welche in einem deskriptiven Evaluationsmodell zu drei Faktoren ($MEQ_{1\text{-}3}$) bzw. einem Gesamtwert (GZi) zusammengefasst werden.

Die in der Arbeit vorgestellten klinischen Outcome-Parameter sind gemäß Leistungsprofil der österreichischen Sozialversicherungsträger in jeder Rehabilitationseinrichtung, bei allen Indikationen, im Rahmen der Ergebnisanalyse eines Patienten im Entlassungsbericht verpflichtend zu dokumentieren. Die Auswahl dieser unspezifischen Outcome-Parameter wird nicht explizit begründet, folgt jedoch evidenzbasierten und ökonomischen Überlegungen, welche einen vergleichbaren medizinischen Qualitätsstandard garantieren sollen. Übergewicht, Bluthochdruck und körperliche Inaktivität sind mit einem schlechteren Gesundheitszustand, Herz-Kreislauferkrankungen und Stoffwechselstörungen assoziiert. Sie gehören zu den wichtigsten veränderbaren Risikofaktoren für chronische Krankheiten und vorzeitigem Tod [43]. Eine wichtige Aufgabe in der stationären Rehabilitation ist es, neben der individuellen symptomatischen Behandlung eines Patienten, diese Risikofaktoren nachhaltig zu reduzieren. Lebensqualität und Funktionsfähigkeit werden durch positiv erlebte Modifikationen des Lebensstils, wie z.B. einer Zunahme der körperlichen Aktivität, gesteigert. Eine Senkung der erfassten klinischen Basiskennwerte, wie BMI, Bauchumfang, Blutdruck, Puls und Schmerzen [44-47] hat daher auch in der stationären Rehabilitation degenerativer, entzündlicher muskuloskelettaler Beschwerden am Stütz- und Bewegungsapparates eine hohe Relevanz [48-50]. Ein rechnerischer Vergleich mit „gesunden" Referenzdaten unterstreicht die Bedeutung der in dieser Arbeit vorgestellten unspezifischen MEQ-Faktoren (MED1-3 & GZi), welche deutlich negative Ausprägungen in den MEQ-Faktoren bei gesunden Menschen erwarten lassen, in der Größenordnung von ca. einer Standardabweichung.

Pseudonymisierte medizinische Routinedaten der Versicherten zur Ergebnisqualität stationär durchgeführter Heilverfahren ermöglichen es, Rehabilitationsmaßnahmen, Struktur- und Prozesslandschaft miteinander in Beziehung zu setzen. Über verschiedene medizinische Kennwerte hinweg werden einfache deskriptive Methoden und monozentrische klinische Referenzdaten vorgestellt, die als Grundlage für das einrichtungsinterne Qualitätsmanagement und zur Gestaltung neuer evidenzbasierter, stratifizierter Behandlungspfade verwendet werden. Mit klinischen Referenzdaten zur WHO - Phase II Rehabilitation wird ein repräsentativer Vergleich mit Gesunden oder Rehabilitanden aus anderen Indikationen möglich. Anhand der vorgestellten zu erwartenden klinischen Änderung können, neben Einrichtungsvergleichen, sehr effizient standardisierte Bewertungen zu unterschiedlichen Behandlungsangeboten durchgeführt werden. Überdies haben bestehende Leistungsprofile einen gewissen Spielraum, um Behandlungsschwerpunkte zu setzten oder vielversprechende Therapiemöglichkeiten anzuwenden. Derartig gestaltete, differenzierte Behandlungspfade sind für eine effiziente und erfolgreiche Behandlung notwendig, damit individuell auf einzelne Patienten bzw. spezifische Patientengruppen eingegangen werden kann. Mit dem vorgestellten Evaluationsmodell am Prüfzentrum hat ein Arzt oder Einrichtung nun auch in der Routineversorgung die Möglichkeit, relativ schnell eine evidenzbasierte Entscheidung zu treffen. Auch potentielle Umwelteinflüsse bzw. eine Änderung von Rahmenbedingungen kann damit hinsichtlich der MEQ evaluiert werden. Die erfassten Routinedaten werden dabei sowohl als Bewertungskriterium als auch als Vergleichsdaten der zu erwartenden MEQ oder Ausgangswerte herangezogen.

Um sinnvoll und deduktiv zu arbeiten ist es hilfreich, die Fülle an teilweise redundanter Information auf ein überschaubares, einheitliches Maß zu reduzieren. Eine additive Zusammenfassung unabhängiger medizinischer Bereiche (Faktoren) zu einer Kennzahl (dem GZi) ist inhaltlich und statistisch zu diskutieren, gibt jedoch einen einfachen und schnellen Überblick zur „unspezifischen" Wirksamkeit des rehabilitativen Aufenthalts für bestimmte Kollektive oder von Behandlungsprogrammen.

Die Betrachtung der zwei vorgestellten Gesundheitsprogramme (ORehab vs. GVA) zeigt, dass die Ausgangswerte zu Rehabilitationsbeginn erwartungsgemäß auf Grund der Zuweisungsbestimmungen zwischen den beiden Teilstichproben nicht unmittelbar vergleichbar sind. AGW-Unterschiede (ohne Berücksichtigung von Lebensalter und Geschlecht) in elementaren medizinischen Messgrößen sind insbesondere bei Bauchumfang, systolischem Blutdruck und in der Schmerzwahrnehmung zu beobachten.

ORehab Patienten haben im Mittel etwas ungünstigere anatomische und physiologische AGW, wobei demgegenüber von GVA-Patienten eine wesentlich höhere Beschwerdeintensität (vgl. VAS-Schmerzen) berichtet wird.

Die Unterschiede zwischen Rehabilitanden mit versus ohne manifeste Erkrankungen des Stütz- und Bewegungsapparates fallen jedoch im Mittel eher gering aus und werden maßgeblich vom Geschlecht und Lebensalter beeinflusst. Dies spricht gegen eine ausreichende Sensitivität allgemeiner medizinischer Outcome-Kennwerte für diese Fragestellung. Andererseits unterstreicht das Ergebnis die Bedeutung der „Zeitdauer des Bestehens" für die Entstehung einer manifesten Erkrankung des Stütz- und Bewegungsapparates sowie die Rolle des Geschlechts. Chronische Erkrankungen haben meist multifaktorielle Ursachen mit einem langfristigen, progredienten Verlauf. Neben genetischen Prädispositionen kommt es bei einer sich wiederholenden oder überdauernden Fehlbeanspruchung, unzureichender Erholung, einem ungesunden Lebensstil und damit einhergehenden erhöhten Risikofaktoren wie z.B. Bluthochdruck und Adipositas zu pathophysiologischen Veränderungen, welche sich auf kardiovaskulärer, endokriner, immunologischer, neurobiologischer und muskuloskelettaler Ebene manifestieren können [vgl. Allostatic Load, 51]. GVA-Patienten befinden sind in diesem Sinne in der „Vorstufe" einer manifesten Erkrankung. Ohne sekundärpräventive Maßnahmen oder Änderungen der Lebens- und Umweltsituation würden sich diese Patienten als zukünftige Akutpatienten im Krankenhaus- und in weiterer Folge in einem Rehabilitationssetting wiederfinden.

Bei der Beurteilung der unspezifischen Wirksamkeit eines rehabilitativen Aufenthalts Maßnahmen anhand allgemeiner Faktoren (MED_{1-3} & GZi) kommen Gruppierungsmerkmalen wie Indikation, Geschlecht und Alter eine geringe Bedeutung zu. Beim Vergleich der Werte vom Ende des Rehabilitationsaufenthalts mit den AGW zeigt sich, dass 74% der Patienten unmittelbar von der stationären Rehabilitation profitieren. Signifikante Wechselwirkungen (WW) mit Gruppierungsmerkmalen sind vorhanden, können jedoch im Vergleich zu den Haupteffekten als „klein" eingestuft werden (η_{WW}^2<.030). Der beobachtete starke Rehabilitationseffekt fällt für alle Subgruppen ähnlich aus (η_{GZi}^2>.500). Dieser unspezifische Erfolg ist vermutlich allen stationären rehabilitativen Aufenthalten gemeinsam und auf den präventiven Effekt von Aktivität bzw. Bewegung und auf das Rehabilitationssetting zurückzuführen.

In der ORehab-Teilstichprobe der Knie- und Hüft-TEP-Patienten mit Wartegruppencharakter zeigt sich, dass die Veränderung in der unspezifischen MEQ unabhängig vom Rehabilitationseintrittszeitpunkt, der post-OP-Woche, erfolgt. In einer unbehandelten „echten" Kontrollgruppe ohne Rehabilitation ist daher keine positive Veränderung des konstitutionellen Gesundheitszustands zu erwarten. Die Bedeutung eines möglichst frühen stationären Rehabilitationsbeginns wird hingegen in (krankheits-)spezifischen Outcome-Kennwerten (z.B. WOMAC, Gehtests) deutlich. Dies unterstreicht die Wichtigkeit einer mehrdimensionalen Betrachtungsweise von spezifischer und unspezifischer Ergebnisqualität, die zwei voneinander unabhängige (Wirk-)Komponenten einer Rehabilitation beschreiben.

Trotz großer Unterschiede in den Kollektiven und Behandlungsmaßnahmen (ORehab versus GVA) unterstützen die beobachteten Effektstärken bei individuellen Evaluierungen, können diese jedoch nicht ersetzen. Neben dem Einzelfall gilt es, den medizinischen Fokus, die rehabilitative Praxis und Leistungsprofile zu berücksichtigen, da die

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statistischen Ergebnisse durch unterschiedliche Behandlungsprogramme und einen damit einhergehenden, unterschiedlichen Ressourceneinsatz zustande kommen.

Absolutwerte und individuelle Profile der MEQ sind immer nach vorliegendem Setting und ärztlichem Ermessen zu bewerten. Einzelmessungen sind mit vielfältigen moderierenden Einflüssen und Messfehlern behaftet.

Bei Verwendung der vorgestellten klinischen Referenzwerte der MEQ für orthopädische Rehabilitanden (WHO - Phase 2) und GVA-Patienten in Österreich ist, neben dem Stichprobenkollektiv, der monozentrische Charakter der Arbeit zu beachten. Die Notwendigkeit einer Adjustierung für Einrichtungsvergleiche kann nicht endgültig beantwortet werden. Unterschiedliche individuelle Ausgangswerte sind immer zu berücksichtigen, denn schlechtere Outcome-Parameter zu Rehabilitationsbeginn gehen mit einem stärkeren Verbesserungspotential einher (z.B. r_{GZi}=-.489; η_{GZi}^2=.243). Auf Grund der vorgeschriebenen Leistungsprofile und der zentral gesteuerten Zuweisungsmodalität durch die Kostenträger ist jedoch davon auszugehen, dass die vorgestellten Ausgangswerte und v.a. die Änderungen in der unspezifischen MEQ repräsentativ für die stationäre Rehabilitation des Stütz- und Bewegungsapparates in Österreich sind.

Die präsentierten kontinuierlichen Messgrößen der MEQ haben gegenüber kategorialen Kriterien Vorteile hinsichtlich ihrer (Skalen-)Eigenschaften und Sensitivität. Eine Verbesserung erfolgt hier in der Regel „unidirektional“. In seltenen Einzelfällen oder auch bei anderen Indikationen, wie in der Onkologischen Rehabilitation, kann eine Verbesserung z.B. eine Gewichtszunahme bedeuten. Hierfür wäre die Skalierung anzupassen, indem Abweichungen von einem (individuellen) Optimalwert als Messgröße herangezogen werden. Das Vorgehen bzw. die Berechnungsmethode der MED-Faktoren müsste dahingehend geringfügig adaptiert werden. In der vorliegenden Eichstichprobe für GVA und ORehab sind jedoch weniger als 0,50% der Rehabilitanden untergewichtig (BMI<18,5; bei 77,2 % ist der BMI>25; vgl. auch Blutdruck: 79,1% der Patienten sind „hoch-normal" bzw. „hyperton").

Die präsentierten Ergebnisse und Erfahrungen des Prüfzentrums sprechen dafür, dass die zu erwartenden Rehabilitationseffekte in den globalen MEQ-Faktoren Allgemeingültigkeit besitzen. Risikoadjustierung bzw. indikations- und gruppenspezifische Modellierungen erscheinen nicht notwendig. Eine nähere Charakterisierung von Non-Responder und Verlaufstypen steht noch aus.

Aus medizinischer Sicht sind vor allem spezifische Merkmale der MEQ von Interesse, wie Leistungsfähigkeit, Funktions-, Aktivitäts- und Partizipationsbeeinträchtigungen bzw. erkrankungs-/verletzungsspezifischen Indikatoren. Die Daten und Ergebnisse dazu sind am Prüfzentrum vorliegend, hätten jedoch den Rahmen dieser Arbeit gesprengt.

Limitation

Die praktische Bedeutung der (indirekten) unspezifischen MEQ-Zielgrößen bzw. Zusammenhänge mit externe Kriterien (Endpunkten), wie Arbeitsunfähigkeitszeiten, sind noch zu prüfen. Vor allem in der Zusammenschau zwischen MEQ und sozialmedizinisch relevanten Außenkriterien besteht Entwicklungspotential. Abzuklären ist, welche der beobachteten Veränderungen in der MEQ Aussagekraft hinsichtlich der Nachhaltigkeit rehabilitativer Maßnahmen haben und inwieweit mit optimierten Behandlungspfaden darauf Einfluss genommen werden kann. Verbesserungen in einem Outcome können dabei durchaus mit Verschlechterungen in anderen Endpunkten einhergehen [41]. Daher sind mehrdimensionale Betrachtungsweisen der Ergebnisqualität immer die Methoden der Wahl.

Kernbotschaft

Neben der gebräuchlichen, „primär patientenseitig" erhobenen Ergebnisqualität, der subjektiven Einschätzung und Zufriedenheit durch Selbstauskunft des Patienten und Qualitätsregistern mit Angaben zu OP-Häufigkeiten, Aufenthaltsdauern und Komplikationen, stellen die vorgestellten unspezifischen Faktoren der Medizinischen Ergebnisqualität eine wertvolle Ergänzung dar. Diese können wesentlich zu Entscheidungs-, Gestaltungsprozessen bzw. Weiterentwicklungen der Qualität in Rehabilitationseinrichtungen beitragen.

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Tabelle 1: Analysestichprobe im Leistungszeitraum 2016-2018.

Tabelle 2: Faktorenbildung der unspezifischen MEQ.

RRsys/dia … systolischer/diastolischer Blutdruck; RP … Ruhepuls; VAS … Visuelle Analog Skala (Schmerz; 0-10); GSZS … Gesundheitszustand (0-100; EQ-VAS); Hohe (positive) Werte [z] entsprechen einem ungünstigeren Wert. PCA (Varimax Rotation): 71% Varianzaufklärung; MED1: 33%, MED2: 21%, MED3: 17%. Die allgemeinen Outcome-Parameter bzw. drei Faktoren zu einem Mittelwert zusammenfasst ergeben den „Gesundheitszustandsindex (GZ_{Index})". Es gibt keine Mehrfachladungen (>.20), die Faktorenstruktur ist stabil.

Tabelle 3: Ausgangswerte GVA vs. ORehab und unspezifische MEQ.

Tabelle 4a: Statistische Kennwerte zu Rehabilitationseffekten (MEQ).

*. (Unspezifische) MEQ-Einzelwerte: BMI, Bauchumfang, Blutdruck, Ruhepuls, Schmerz (VAS), subj. Gesundheitszustand (EQ-VAS); **. (Unspezifische) MEQ-Faktoren: MED1, MED2, MED3 und GZi [z]; *HE: Haupteffekt; WW: Wechselwirkung; Kov. … Kovariate;*

Tabelle 4b: Teilstichprobe ORehab - "spezifische" EQ vs. "unspezifische" MEQ.

HE: Haupteffekt; *. Spezifische Ergebnisqualität (EQ): WOMAC Summenscore [0-240], Gehtests [sec]: Time up & go, 10m Gehtest und Beeinträchtigungen/ADL (EQ5D-3L; Summenmodell) [0-100]; **. Unspezifische MEQ-Faktoren: MED1, MED2, MED3 und GZi [z];

Tabelle 5: Allgemeine Ergebnisqualität.

*. AGW… Ausgangswert zu Rehabilitationsbeginn: Ein negativer %-Wert entspricht einem unterdurchschnittlichen (schlechteren) Wert in der Gesamtstichprobe. Ein AGW (Perzentil) um Null bedeutet, dass kein Unterschied zur Gesamtstichprobe besteht (hier: Patienten mit muskuloskelettalen Beschwerden; GVA und ORehab-Patienten) bzw. gibt Auskunft zur Abweichung der Verteilung von einer Normalverteilung. **. Durchschnittliche Perzentilverbesserung von Aufnahme- zu Entlassungszeitpunkt; BMI… Body Mass Index, BD… Blutdruck, RP… Ruhepuls, VAS… Visuelle Analog Skala (Schmerz), GSZS… Gesundheitszustand (EQ-VAS);

Tabelle 6a: MEQ-Faktor-Referenzwerte zu Rehabilitationsbeginn (AGW).

*. Positivere (z-)Werte entsprechen hier einem schlechteren Wert (AGW) zum Aufnahmezeitpunkt; **. CI … Vertrauensintervall (+/- 1 SD).

Tabelle 6b: MEQ-Faktor-Referenzwerte zu Rehabilitationsende und Rehaberfolg.

*. Negative (z-Differenz-) Werte entsprechen hier einer Verbesserung von Aufnahme zu Entlassung; **. Absolutwerte (z) - negativere Werte entsprechen einer stärkeren Verbesserung; SD … Standardabweichung. Anmerkung: Die Korrelationen der MEQ-Faktoren mit dem Alter sind stabil bzw. sind diese bei Aufnahme- und Entlassungswerten identisch (nicht dargestellt). Der Zusammenhang des Lebensalters mit den Differenzwerten geht gegen Null. Die individuellen Ausgangswerte (AGW) zeigen den zu erwartenden Zusammenhang mit den Differenzwerten (D; E – AGW) in einer Größenordnung von $r_{GZi\ (AGW\ vs.\ E-AGW)}$=-.489. D.h. schlechtere Ausgangswerte zu Rehabilitationsbeginn gehen im Einzelfall mit einer stärkeren Veränderung (Verbesserung) einher.

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